

# Search history

Krishnan 10/786613

02/22/2006

=> d his full

(FILE 'HOME' ENTERED AT 11:58:08 ON 22 FEB 2006)

FILE 'REGISTRY' ENTERED AT 11:58:19 ON 22 FEB 2006

L1 STRUCTURE UPLOADED  
L2 50 SEA SSS SAM L1  
D STAT QUE L2  
L3 1062 SEA SSS FUL L1  
SAVE TEMP L3 KRI613STRB/A  
L4 330 SEA ABB=ON PLU=ON L3 AND NC>1  
L5 330 SEA ABB=ON PLU=ON L3 AND NC=2  
L6 305 SEA ABB=ON PLU=ON L4 AND NA>0  
L7 25 SEA ABB=ON PLU=ON L4 NOT L6  
L8 STRUCTURE UPLOADED  
L9 4 SEA SUB=L3 SSS SAM L8  
D SCA  
D STAT QUE L9  
L10 79 SEA SUB=L3 SSS FUL L8  
SAVE TEMP L10 KRI613STRA/A

FILE 'CAPLUS' ENTERED AT 12:08:56 ON 22 FEB 2006

L11 33 SEA ABB=ON PLU=ON L10

FILE 'REGISTRY' ENTERED AT 12:09:09 ON 22 FEB 2006

FILE 'STNGUIDE' ENTERED AT 12:09:47 ON 22 FEB 2006

FILE 'REGISTRY' ENTERED AT 12:11:05 ON 22 FEB 2006

L12 STRUCTURE UPLOADED  
L13 11 SEA SUB=L3 SSS SAM L12  
D STAT QUE L13  
L14 226 SEA SUB=L3 SSS FUL L12  
SAVE TEMP L14 KRI613STRC/A  
L15 60 SEA ABB=ON PLU=ON L14 AND NC>1  
L16 60 SEA ABB=ON PLU=ON L15 AND NA>0  
L17 60 SEA ABB=ON PLU=ON L16 AND NC=2  
L18 STRUCTURE UPLOADED  
L19 4 SEA SUB=L3 SSS SAM L18  
L20 79 SEA SUB=L3 SSS FUL L18  
SAVE TEMP L20 KRI613STRD/A

FILE 'CAPLUS' ENTERED AT 12:36:19 ON 22 FEB 2006

L21 33 SEA ABB=ON PLU=ON L20  
L22 9 SEA ABB=ON PLU=ON L2 (L) (THU OR DMA OR PAC OR PKT OR  
BAC)/RL  
D SCA TI L22  
L23 25 SEA ABB=ON PLU=ON ACHARAN SULFATE/OBI  
L24 2 SEA ABB=ON PLU=ON L21 AND L23

FILE 'REGISTRY' ENTERED AT 12:39:34 ON 22 FEB 2006

E ACHARAN/CN  
L25 1 SEA ABB=ON PLU=ON ACHARAN SULFATE/CN  
D SCA  
L26 1 SEA ABB=ON PLU=ON ACHARAN, N-DEACETYL-N-SULFO?/CN  
D SCA

FILE 'CAPLUS' ENTERED AT 12:41:43 ON 22 FEB 2006

L27 24 SEA ABB=ON PLU=ON L25  
L28 5 SEA ABB=ON PLU=ON L26

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L29 2 SEA ABB=ON PLU=ON L21 AND L27  
L30 0 SEA ABB=ON PLU=ON L21 AND L28  
E US2004-786613/APPS  
L31 1 SEA ABB=ON PLU=ON US2004-786613/AP  
SEL RN

FILE 'REGISTRY' ENTERED AT 12:44:41 ON 22 FEB 2006  
L32 1 SEA ABB=ON PLU=ON 192662-57-0/BI  
D SCA

FILE 'CAPLUS' ENTERED AT 12:45:30 ON 22 FEB 2006  
D IALL L31  
E CANCER+ALL/CT  
E E2  
L33 28 SEA ABB=ON PLU=ON ACHARAN?/BI  
L34 51 SEA ABB=ON PLU=ON ?ACHARAN?/BI  
L35 23 SEA ABB=ON PLU=ON L34 NOT L33  
D SCA

FILE 'REGISTRY' ENTERED AT 12:52:37 ON 22 FEB 2006  
E ACHARAN/CN

FILE 'CAPLUS' ENTERED AT 12:53:13 ON 22 FEB 2006  
L36 28 SEA ABB=ON PLU=ON L33 OR L27 OR L28 OR L23  
SAVE TEMP L36 KRI613ACHA/A

FILE 'REGISTRY' ENTERED AT 12:55:22 ON 22 FEB 2006  
SAVE TEMP L17 KRI613MONO/A

FILE 'CAPLUS' ENTERED AT 12:56:43 ON 22 FEB 2006  
SAVE TEMP L31 KRI613APP/A

FILE 'REGISTRY' ENTERED AT 12:57:46 ON 22 FEB 2006  
D SCA L32

FILE 'CAPLUS' ENTERED AT 12:57:54 ON 22 FEB 2006  
L\*\*\* DEL 24 S L32

FILE 'STNGUIDE' ENTERED AT 12:58:58 ON 22 FEB 2006  
D SAV

FILE 'STNGUIDE' ENTERED AT 12:59:48 ON 22 FEB 2006

FILE 'EMBASE' ENTERED AT 13:09:20 ON 22 FEB 2006  
E NEOPLASM+ALL/CT  
E ANGIOGENESIS INHIBITOR+ALL/CT  
E ANTITUMOR AGENT+ALL/CT  
E E2+ALL

FILE 'MEDLINE' ENTERED AT 13:12:51 ON 22 FEB 2006  
E ANTITUMOR AGENTS/CT  
E ANTITUMOR AGENTS+ALL/CT  
E E2=ALL  
E ANTITUMOR AGENTS+ALL/CT  
E E2+ALL  
E E1+ALL/CT

FILE 'STNGUIDE' ENTERED AT 13:13:44 ON 22 FEB 2006

FILE 'CAPLUS' ENTERED AT 13:14:00 ON 22 FEB 2006

E NEOPLASMS+ALL/CT

FILE 'STNGUIDE' ENTERED AT 13:16:47 ON 22 FEB 2006

FILE 'CAPLUS' ENTERED AT 13:17:00 ON 22 FEB 2006

E ANGIOGENESIS INHIBITORS+ALL/CT  
E ANGIOGENESIS INHIBITORS+ALL/CT  
E E10+ALL

FILE 'STNGUIDE' ENTERED AT 13:18:24 ON 22 FEB 2006

FILE 'CAPLUS' ENTERED AT 14:33:01 ON 22 FEB 2006

L37 304372 SEA ABB=ON PLU=ON ?CANCER?/BI  
L38 526763 SEA ABB=ON PLU=ON ?TUMOR?/BI  
L39 3949 SEA ABB=ON PLU=ON ?TUMOUR?/BI  
L40 49768 SEA ABB=ON PLU=ON ?SARCOMA?/BI  
L41 444230 SEA ABB=ON PLU=ON ?NEOPLAS?/BI  
L42 251331 SEA ABB=ON PLU=ON ?CARCINO?/BI  
L43 34965 SEA ABB=ON PLU=ON ?ANGIOGEN?/BI  
L44 7 SEA ABB=ON PLU=ON (L37 OR L38 OR L39 OR L40 OR L41 OR L42)  
AND (L21 OR L22 OR L36)  
L45 4 SEA ABB=ON PLU=ON L43 AND (L21 OR L22 OR L36)  
L46 422 SEA ABB=ON PLU=ON LINHARDT R?/AU  
L47 31492 SEA ABB=ON PLU=ON KIM Y?/AU  
L48 35 SEA ABB=ON PLU=ON L46 AND L47  
L49 13 SEA ABB=ON PLU=ON L48 AND (L21 OR L22 OR L36)

FILE 'REGISTRY' ENTERED AT 14:40:58 ON 22 FEB 2006

SET SMARTSELECT ON

L\*\*\* DEL SEL L20 1- CHEM : 80 TERMS  
SET SMARTSELECT OFF

FILE 'CAPLUS' ENTERED AT 14:41:10 ON 22 FEB 2006

FILE 'REGISTRY' ENTERED AT 14:41:10 ON 22 FEB 2006

SET SMARTSELECT ON

L\*\*\* DEL SEL L25 1- CHEM : 2 TERMS  
SET SMARTSELECT OFF

FILE 'CAPLUS' ENTERED AT 14:41:11 ON 22 FEB 2006

FILE 'REGISTRY' ENTERED AT 14:41:11 ON 22 FEB 2006

SET SMARTSELECT ON

L\*\*\* DEL SEL L26 1- CHEM : 2 TERMS  
SET SMARTSELECT OFF

FILE 'CAPLUS' ENTERED AT 14:41:12 ON 22 FEB 2006

FILE 'MEDLINE' ENTERED AT 14:42:30 ON 22 FEB 2006

L50 18 SEA ABB=ON PLU=ON ACHARAN?  
L51 0 SEA ABB=ON PLU=ON L20  
L52 0 SEA ABB=ON PLU=ON L25  
L53 0 SEA ABB=ON PLU=ON L26

FILE 'REGISTRY' ENTERED AT 14:43:49 ON 22 FEB 2006

SET SMARTSELECT ON

L54 SEL PLU=ON L20 1- CHEM : 80 TERMS  
SET SMARTSELECT OFF

FILE 'MEDLINE' ENTERED AT 14:43:56 ON 22 FEB 2006

L55           0 SEA ABB=ON   PLU=ON   L54

FILE 'REGISTRY' ENTERED AT 14:44:15 ON 22 FEB 2006  
SET SMARTSELECT ON

L56           SEL PLU=ON   L25 1- CHEM :       2 TERMS  
SET SMARTSELECT OFF

FILE 'MEDLINE' ENTERED AT 14:44:16 ON 22 FEB 2006

L57           18 SEA ABB=ON   PLU=ON   L56

FILE 'REGISTRY' ENTERED AT 14:44:25 ON 22 FEB 2006  
SET SMARTSELECT ON

L58           SEL PLU=ON   L26 1- CHEM :       2 TERMS  
SET SMARTSELECT OFF

FILE 'MEDLINE' ENTERED AT 14:44:26 ON 22 FEB 2006

L59           4 SEA ABB=ON   PLU=ON   L58  
L60           18 SEA ABB=ON   PLU=ON   L50 OR L57 OR L59  
L61           579828 SEA ABB=ON   PLU=ON   ?CANCER?  
L62           790107 SEA ABB=ON   PLU=ON   ?TUMOR?  
L63           133927 SEA ABB=ON   PLU=ON   ?TUMOUR?  
L64           125245 SEA ABB=ON   PLU=ON   ?SARCOMA?  
L65           1548799 SEA ABB=ON   PLU=ON   ?NEOPLAS?  
L66           575010 SEA ABB=ON   PLU=ON   ?CARCINO?  
L67           1627678 SEA ABB=ON   PLU=ON   NEOPLASMS+NT/CT  
L68           3636 SEA ABB=ON   PLU=ON   ANGIOGENESIS INHIBITORS/CT  
L69           4 SEA ABB=ON   PLU=ON   L60 AND (L61 OR L62 OR L63 OR L64 OR L65  
OR L66 OR L67 OR L68)  
L70           14 SEA ABB=ON   PLU=ON   L60 NOT L69  
D TRIAL 1-14  
L71           30590 SEA ABB=ON   PLU=ON   ?ANGIOGEN?  
L72           2 SEA ABB=ON   PLU=ON   L60 AND L71  
D TRIAL 1-2  
L73           283 SEA ABB=ON   PLU=ON   LINHARDT R?/AU  
L74           10317 SEA ABB=ON   PLU=ON   KIM Y?/AU  
L75           31 SEA ABB=ON   PLU=ON   L73 AND L74  
L76           9 SEA ABB=ON   PLU=ON   L75 AND L60

FILE 'EMBASE' ENTERED AT 14:51:58 ON 22 FEB 2006

L77           16 SEA ABB=ON   PLU=ON   ACHARAN?  
L78           0 SEA ABB=ON   PLU=ON   L20  
L79           0 SEA ABB=ON   PLU=ON   L25  
L80           0 SEA ABB=ON   PLU=ON   L26

FILE 'REGISTRY' ENTERED AT 14:52:47 ON 22 FEB 2006  
SET SMARTSELECT ON

L81           SEL PLU=ON   L20 1- CHEM :       80 TERMS  
SET SMARTSELECT OFF

FILE 'EMBASE' ENTERED AT 14:52:49 ON 22 FEB 2006

L82           0 SEA ABB=ON   PLU=ON   L81

FILE 'REGISTRY' ENTERED AT 14:52:57 ON 22 FEB 2006  
SET SMARTSELECT ON

L83           SEL PLU=ON   L25 1- CHEM :       2 TERMS  
SET SMARTSELECT OFF

FILE 'EMBASE' ENTERED AT 14:52:57 ON 22 FEB 2006

L84           16 SEA ABB=ON   PLU=ON   L83

FILE 'REGISTRY' ENTERED AT 14:53:04 ON 22 FEB 2006

L85 SET SMARTSELECT ON  
SEL PLU=ON L26 1- CHEM : 2 TERMS  
SET SMARTSELECT OFF

FILE 'EMBASE' ENTERED AT 14:53:05 ON 22 FEB 2006

L86 4 SEA ABB=ON PLU=ON L85  
L87 16 SEA ABB=ON PLU=ON L77 OR L84 OR L86  
L88 851781 SEA ABB=ON PLU=ON ?CANCER?  
L89 778474 SEA ABB=ON PLU=ON ?TUMOR? OR ?TUMOUR?  
L90 90530 SEA ABB=ON PLU=ON ?SARCOMA?  
L91 230147 SEA ABB=ON PLU=ON ?NEOPLAS?  
L92 517907 SEA ABB=ON PLU=ON ?CARCINO?  
L93 34532 SEA ABB=ON PLU=ON ?ANGIOGEN?  
L94 1349056 SEA ABB=ON PLU=ON NEOPLASM+NT/CT  
L95 4217 SEA ABB=ON PLU=ON ANGIOGENESIS INHIBITOR/CT  
L96 4 SEA ABB=ON PLU=ON L87 AND (L88 OR L89 OR L90 OR L91 OR L92  
OR L93 OR L94 OR L95)  
D TRIAL 1-4  
L97 261 SEA ABB=ON PLU=ON LINHARDT R?/AU  
L98 8968 SEA ABB=ON PLU=ON KIM Y?/AU  
L99 21 SEA ABB=ON PLU=ON L97 AND L98  
L100 7 SEA ABB=ON PLU=ON L99 AND (L96 OR L87)

FILE 'BIOSIS' ENTERED AT 14:57:42 ON 22 FEB 2006

L101 22 SEA ABB=ON PLU=ON ACHARAN?  
L102 0 SEA ABB=ON PLU=ON L20  
L103 17 SEA ABB=ON PLU=ON L25  
L104 1 SEA ABB=ON PLU=ON L26

FILE 'REGISTRY' ENTERED AT 14:58:11 ON 22 FEB 2006

L105 SET SMARTSELECT ON  
SEL PLU=ON L20 1- CHEM : 80 TERMS  
SET SMARTSELECT OFF

FILE 'BIOSIS' ENTERED AT 14:58:13 ON 22 FEB 2006

L106 0 SEA ABB=ON PLU=ON L105

FILE 'REGISTRY' ENTERED AT 14:58:21 ON 22 FEB 2006

L107 SET SMARTSELECT ON  
SEL PLU=ON L25 1- CHEM : 2 TERMS  
SET SMARTSELECT OFF

FILE 'BIOSIS' ENTERED AT 14:58:22 ON 22 FEB 2006

L108 21 SEA ABB=ON PLU=ON L107

FILE 'REGISTRY' ENTERED AT 14:58:29 ON 22 FEB 2006

L109 SET SMARTSELECT ON  
SEL PLU=ON L26 1- CHEM : 2 TERMS  
SET SMARTSELECT OFF

FILE 'BIOSIS' ENTERED AT 14:58:30 ON 22 FEB 2006

L110 4 SEA ABB=ON PLU=ON L109  
L111 22 SEA ABB=ON PLU=ON L101 OR L103 OR L104 OR L108 OR L110  
L112 546518 SEA ABB=ON PLU=ON ?CANCER?  
L113 976062 SEA ABB=ON PLU=ON ?TUMOR? OR ?TUMOUR?  
L114 95426 SEA ABB=ON PLU=ON ?SARCOMA?  
L115 759144 SEA ABB=ON PLU=ON ?NEOPLAS?  
L116 507193 SEA ABB=ON PLU=ON ?CARCINO?  
L117 35893 SEA ABB=ON PLU=ON ?ANGIOGEN?

E NEOPLASM+ALL/CT  
E E3+ALL  
L118 4 SEA ABB=ON PLU=ON L111 AND (L112 OR L113 OR L114 OR L115 OR  
L116 OR L117)  
L119 18 SEA ABB=ON PLU=ON L111 NOT L118  
L120 359 SEA ABB=ON PLU=ON LINHARDT R?/AU  
L121 15625 SEA ABB=ON PLU=ON KIM Y?/AU  
L122 40 SEA ABB=ON PLU=ON L120 AND L121  
L123 11 SEA ABB=ON PLU=ON L122 AND (L111 OR L118)

FILE 'USPATFULL' ENTERED AT 15:05:15 ON 22 FEB 2006

L124 1 SEA ABB=ON PLU=ON L20  
L125 2 SEA ABB=ON PLU=ON L25  
L126 1 SEA ABB=ON PLU=ON L26

FILE 'REGISTRY' ENTERED AT 15:06:18 ON 22 FEB 2006

SET SMARTSELECT ON  
L127 SEL PLU=ON L20 1- CHEM : 80 TERMS  
SET SMARTSELECT OFF

FILE 'USPATFULL' ENTERED AT 15:06:20 ON 22 FEB 2006

L128 0 SEA ABB=ON PLU=ON L127

FILE 'REGISTRY' ENTERED AT 15:06:30 ON 22 FEB 2006

SET SMARTSELECT ON  
L129 SEL PLU=ON L25 1- CHEM : 2 TERMS  
SET SMARTSELECT OFF

FILE 'USPATFULL' ENTERED AT 15:06:30 ON 22 FEB 2006

L130 4 SEA ABB=ON PLU=ON L129

FILE 'REGISTRY' ENTERED AT 15:06:36 ON 22 FEB 2006

SET SMARTSELECT ON  
L131 SEL PLU=ON L26 1- CHEM : 2 TERMS  
SET SMARTSELECT OFF

FILE 'USPATFULL' ENTERED AT 15:06:36 ON 22 FEB 2006

L132 1 SEA ABB=ON PLU=ON L131  
L133 4 SEA ABB=ON PLU=ON ACHARAN?  
L134 5 SEA ABB=ON PLU=ON L124 OR L125 OR L126 OR L130 OR L132 OR  
L133  
L135 120107 SEA ABB=ON PLU=ON ?CANCER?  
L136 104777 SEA ABB=ON PLU=ON ?TUMOR?  
L137 12054 SEA ABB=ON PLU=ON ?TUMOUR?  
L138 34800 SEA ABB=ON PLU=ON ?SARCOMA?  
L139 37564 SEA ABB=ON PLU=ON ?NEOPLAS?  
L140 67199 SEA ABB=ON PLU=ON ?CARCINO?  
L141 22227 SEA ABB=ON PLU=ON ?ANGIOGEN?  
L142 4 SEA ABB=ON PLU=ON L134 AND (L135 OR L136 OR L137 OR L138 OR  
L139 OR L140 OR L141)  
L143 1 SEA ABB=ON PLU=ON L134 NOT L142  
D SCA  
L144 28 SEA ABB=ON PLU=ON LINHARDT R?/AU  
L145 4380 SEA ABB=ON PLU=ON KIM Y?/AU  
L146 2 SEA ABB=ON PLU=ON L144 AND L145  
L147 2 SEA ABB=ON PLU=ON L146 AND L142

FILE 'STNGUIDE' ENTERED AT 15:11:50 ON 22 FEB 2006

FILE 'REGISTRY' ENTERED AT 15:13:00 ON 22 FEB 2006

L\*\*\* DEL 0 S L20 AND RELATED POLYMERS/FA  
L\*\*\* DEL 0 S L\*\*\*  
L148 79 POLYLINK L20  
L149 0 SEA ABB=ON PLU=ON L148 NOT L20

FILE 'STNGUIDE' ENTERED AT 15:14:33 ON 22 FEB 2006

FILE 'REGISTRY' ENTERED AT 15:14:46 ON 22 FEB 2006  
D STAT QUE L17  
D STAT QUE L20  
D QUE NOS L149

FILE 'STNGUIDE' ENTERED AT 15:15:59 ON 22 FEB 2006

FILE 'WPIX' ENTERED AT 15:20:01 ON 22 FEB 2006

L150 0 SEA SSS SAM L18  
L151 1 SEA SSS FUL L18

FILE 'STNGUIDE' ENTERED AT 15:20:34 ON 22 FEB 2006

FILE 'WPIX' ENTERED AT 15:22:23 ON 22 FEB 2006

L152 1 SEA ABB=ON PLU=ON L151/DCR  
L153 28 SEA ABB=ON PLU=ON LINHARDT R?/AU  
L154 28293 SEA ABB=ON PLU=ON KIM Y?/AU  
L155 2 SEA ABB=ON PLU=ON L153 AND L154  
L156 5 SEA ABB=ON PLU=ON ACHARAN?  
L157 119623 SEA ABB=ON PLU=ON (L135 OR L136 OR L137 OR L138 OR L139 OR  
L140 OR L141)  
L158 0 SEA ABB=ON PLU=ON L152 AND L157  
L159 3 SEA ABB=ON PLU=ON L156 AND L157  
L160 2 SEA ABB=ON PLU=ON L155 AND (L152 OR L156)

FILE 'STNGUIDE' ENTERED AT 15:25:47 ON 22 FEB 2006

FILE 'CAPLUS' ENTERED AT 15:30:55 ON 22 FEB 2006  
D QUE NOS L48  
D QUE NOS L49

L161 35 SEA ABB=ON PLU=ON (L48 OR L49)

FILE 'MEDLINE' ENTERED AT 15:30:58 ON 22 FEB 2006

D QUE NOS L75  
D QUE NOS L76  
L162 31 SEA ABB=ON PLU=ON (L75 OR L76)

FILE 'EMBASE' ENTERED AT 15:31:01 ON 22 FEB 2006

D QUE NOS L99  
D QUE NOS L100  
L163 21 SEA ABB=ON PLU=ON (L99 OR L100)

FILE 'BIOSIS' ENTERED AT 15:31:04 ON 22 FEB 2006

D QUE NOS L122  
D QUE NOS L123  
L164 40 SEA ABB=ON PLU=ON (L122 OR L123)

FILE 'WPIX' ENTERED AT 15:31:07 ON 22 FEB 2006

D QUE NOS L155  
D QUE NOS L160  
L165 2 SEA ABB=ON PLU=ON L155 OR L160

FILE 'USPATFULL' ENTERED AT 15:31:11 ON 22 FEB 2006

L166 D QUE NOS L146  
D QUE NOS L147  
2 SEA ABB=ON PLU=ON L146 OR L147

FILE 'STNGUIDE' ENTERED AT 15:31:22 ON 22 FEB 2006

FILE 'CAPLUS, MEDLINE, EMBASE, BIOSIS, WPIX, USPATFULL' ENTERED AT  
15:32:34 ON 22 FEB 2006

L167 47 DUP REM L161 L162 L163 L164 L165 L166 (84 DUPLICATES REMOVED)  
ANSWERS '1-35' FROM FILE CAPLUS  
ANSWERS '36-37' FROM FILE MEDLINE  
ANSWERS '38-46' FROM FILE BIOSIS  
ANSWER '47' FROM FILE USPATFULL  
D IBIB ABS HITIND HITSTR L167 1-35  
D IALL L167 36-46  
D IBIB ABS KWIC HITSTR L167 47

FILE 'STNGUIDE' ENTERED AT 15:34:54 ON 22 FEB 2006

FILE 'CAPLUS' ENTERED AT 15:40:05 ON 22 FEB 2006  
D QUE NOS L44  
D QUE NOS L45

L168 4 SEA ABB=ON PLU=ON ((L44 OR L45)) NOT L161

FILE 'MEDLINE' ENTERED AT 15:40:08 ON 22 FEB 2006  
D QUE NOS L51  
D QUE NOS L52  
D QUE NOS L53  
D QUE NOS L55  
D QUE NOS L69  
D QUE NOS L72

L169 3 SEA ABB=ON PLU=ON ((L51 OR L52 OR L53) OR L55 OR L69 OR L72)  
NOT L162

FILE 'EMBASE' ENTERED AT 15:40:14 ON 22 FEB 2006  
D QUE NOS L78  
D QUE NOS L79  
D QUE NOS L80  
D QUE NOS L82  
D QUE NOS L96

L170 2 SEA ABB=ON PLU=ON (L78 OR L79 OR L80 OR L82 OR L96) NOT L163

FILE 'BIOSIS' ENTERED AT 15:40:19 ON 22 FEB 2006  
D QUE NOS L102  
D QUE NOS L106  
D QUE NOS L118

L171 2 SEA ABB=ON PLU=ON (L102 OR L106 OR L118) NOT L164

FILE 'WPIX' ENTERED AT 15:40:23 ON 22 FEB 2006  
D QUE NOS L159  
D QUE NOS L152  
D QUE NOS L158

L172 2 SEA ABB=ON PLU=ON (L159 OR L152 OR L158) NOT L165

FILE 'USPATFULL' ENTERED AT 15:40:28 ON 22 FEB 2006  
D QUE NOS L128  
D QUE NOS L142

L173 2 SEA ABB=ON PLU=ON (L128 OR L142) NOT L166



FILE 'STNGUIDE' ENTERED AT 15:40:45 ON 22 FEB 2006

FILE 'CAPLUS, MEDLINE, EMBASE, BIOSIS, WPIX, USPATFULL' ENTERED AT 15:42:45 ON 22 FEB 2006

L174 8 DUP REM L168 L169 L170 L171 L172 L173 (7 DUPLICATES REMOVED)  
ANSWERS '1-4' FROM FILE CAPLUS  
ANSWER '5' FROM FILE MEDLINE  
ANSWER '6' FROM FILE WPIX  
ANSWERS '7-8' FROM FILE USPATFULL  
D IBIB ABS HITIND HITSTR L174 1-4  
D IALL L174 5  
D IBIB ABS HITSTR L174 6  
D IBIB ABS KWIC HITSTR L174 7-8

FILE HOME

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 20 FEB 2006 HIGHEST RN 874742-76-4

DICTIONARY FILE UPDATES: 20 FEB 2006 HIGHEST RN 874742-76-4

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

\*\*\*\*\*  
\*  
\* The CA roles and document type information have been removed from \*  
\* the IDE default display format and the ED field has been added, \*  
\* effective March 20, 2005. A new display format, IDERL, is now \*  
\* available and contains the CA role and document type information. \*  
\*  
\*\*\*\*\*

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

FILE CAPLUS

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FILE COVERS 1907 - 22 Feb 2006 VOL 144 ISS 9  
FILE LAST UPDATED: 21 Feb 2006 (20060221/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.  
They are available for your review at:

<http://www.cas.org/infopolicy.html>

FILE STNGUIDE  
FILE CONTAINS CURRENT INFORMATION.  
LAST RELOADED: Feb 17, 2006 (20060217/UP).

FILE EMBASE  
FILE COVERS 1974 TO 20 Feb 2006 (20060220/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

FILE MEDLINE  
FILE LAST UPDATED: 21 FEB 2006 (20060221/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 will soon be available. For details  
on the 2005 reload, enter HELP RLOAD at an arrow prompt (=>).  
See also:

<http://www.nlm.nih.gov/mesh/>  
[http://www.nlm.nih.gov/pubs/techbull/nd04/nd04\\_mesh.html](http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html)  
[http://www.nlm.nih.gov/pubs/techbull/nd05/nd05\\_med\\_data\\_changes.html](http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html)  
[http://www.nlm.nih.gov/pubs/techbull/nd05/nd05\\_2006\\_Mesh.html](http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_Mesh.html)

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the  
MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate

FILE BIOSIS  
FILE COVERS 1969 TO DATE.  
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT  
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 15 February 2006 (20060215/ED)

FILE USPATFULL  
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 21 Feb 2006 (20060221/PD)  
FILE LAST UPDATED: 21 Feb 2006 (20060221/ED)  
HIGHEST GRANTED PATENT NUMBER: US7003800  
HIGHEST APPLICATION PUBLICATION NUMBER: US2006037120  
CA INDEXING IS CURRENT THROUGH 21 Feb 2006 (20060221/UPCA)  
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 21 Feb 2006 (20060221/PD)  
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2005  
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2005

FILE WPIX

FILE LAST UPDATED: 17 FEB 2006 <20060217/UP>

MOST RECENT DERWENT UPDATE: 200612 <200612/DW>

DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,  
PLEASE VISIT:

[http://www.stn-international.de/training\\_center/patents/stn\\_guide.pdf](http://www.stn-international.de/training_center/patents/stn_guide.pdf) <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE  
<http://scientific.thomson.com/support/patents/coverage/latestupdates/>

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER  
GUIDES, PLEASE VISIT:

<http://scientific.thomson.com/support/products/dwpi/>

>>> FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT  
DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX  
FIRST VIEW - FILE WPIFV.  
FOR FURTHER DETAILS:

<http://scientific.thomson.com/support/products/dwpifv/>

>>> THE CPI AND EPI MANUAL CODES WILL BE REVISED FROM UPDATE 200601.  
PLEASE CHECK:

<http://scientific.thomson.com/support/patents/dwpieref/reftools/classificat>

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE  
[http://www.stn-international.de/stndatabases/details/ipc\\_reform.html](http://www.stn-international.de/stndatabases/details/ipc_reform.html) and  
<http://scientific.thomson.com/media/scpdf/ipcrdwpf.pdf> <<<

=>

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=> file registry

FILE 'REGISTRY' ENTERED AT 15:14:46 ON 22 FEB 2006

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 21 FEB 2006 HIGHEST RN 874882-62-9

DICTIONARY FILE UPDATES: 21 FEB 2006 HIGHEST RN 874882-62-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

```
*****
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*
*****
```

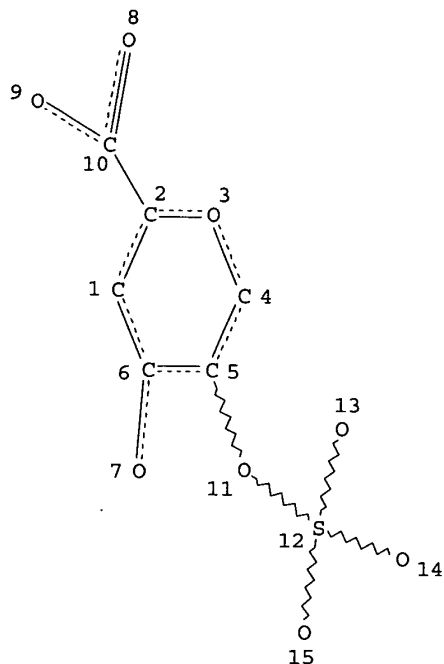
Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=> d stat que L17

L1 STR



## NODE ATTRIBUTES:

|                            |          |    |                         |
|----------------------------|----------|----|-------------------------|
| NSPEC                      | IS R     | AT | 1                       |
| NSPEC                      | IS R     | AT | 2                       |
| NSPEC                      | IS R     | AT | 3                       |
| NSPEC                      | IS R     | AT | 4                       |
| NSPEC                      | IS R     | AT | 5                       |
| NSPEC                      | IS R     | AT | 6                       |
| NSPEC                      | IS C     | AT | 7                       |
| NSPEC                      | IS C     | AT | 8                       |
| NSPEC                      | IS C     | AT | 9                       |
| NSPEC                      | IS C     | AT | 10                      |
| NSPEC                      | IS C     | AT | 11                      |
| NSPEC                      | IS C     | AT | 12                      |
| NSPEC                      | IS C     | AT | 13                      |
| NSPEC                      | IS C     | AT | 14                      |
| NSPEC                      | IS C     | AT | 15                      |
| CONNECT                    | IS E3    | RC | AT 10                   |
| DEFAULT MLEVEL IS ATOM     |          |    |                         |
| MLEVEL                     | IS CLASS | AT | 7 8 9 10 11 12 13 14 15 |
| DEFAULT ECLEVEL IS LIMITED |          |    |                         |

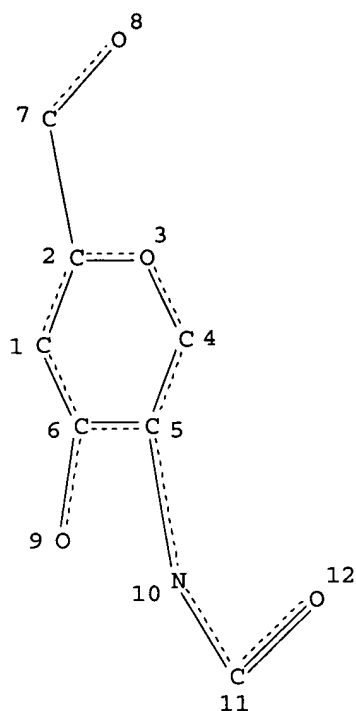
## GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 15

## STEREO ATTRIBUTES: NONE

L3 1062 SEA FILE=REGISTRY SSS FUL L1  
 L12 STR

← registry #s that  
 contain the  
 sulfur-containing 1/2  
 of the repeating unit.



## NODE ATTRIBUTES:

```

NSPEC   IS R      AT    1
NSPEC   IS R      AT    2
NSPEC   IS R      AT    3
NSPEC   IS R      AT    4
NSPEC   IS R      AT    5
NSPEC   IS R      AT    6
NSPEC   IS C      AT    7
NSPEC   IS C      AT    8
NSPEC   IS C      AT    9
NSPEC   IS C      AT   10
NSPEC   IS C      AT   11
NSPEC   IS C      AT   12
DEFAULT MLEVEL IS ATOM
MLEVEL   IS CLASS AT    7  8  9 10 11 12
DEFAULT ECLEVEL IS LIMITED

```

## GRAPH ATTRIBUTES:

```

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 12

```

## STEREO ATTRIBUTES: NONE

```

L14      226 SEA FILE=REGISTRY SUB=L3 SSS FUL L12
L15      60 SEA FILE=REGISTRY ABB=ON  PLU=ON  L14 AND NC>1
L16      60 SEA FILE=REGISTRY ABB=ON  PLU=ON  L15 AND NA>0
L17      60 SEA FILE=REGISTRY ABB=ON  PLU=ON  L16 AND NC=2

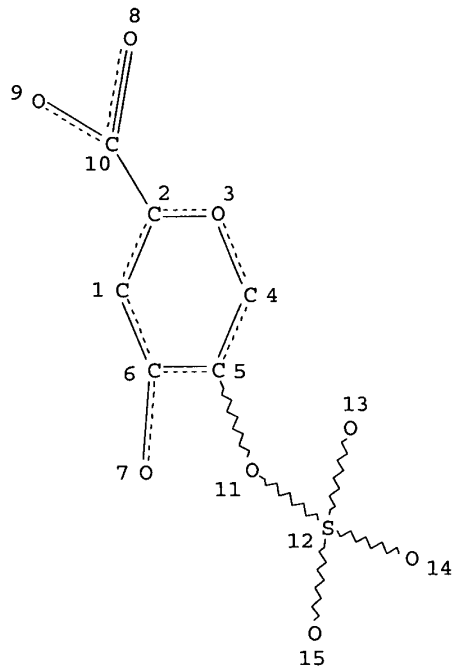
```

```

=> d stat que L20
L1          STR

```

← registry numbers that  
 contain both ~~the~~  
 halves of the  
 containing unit  
 query  
 logic shows that  
 all entries that contain  
 2 components contain  
 sodium not 2 monomer  
 units.



## NODE ATTRIBUTES:

|                            |    |       |    |                         |
|----------------------------|----|-------|----|-------------------------|
| NSPEC                      | IS | R     | AT | 1                       |
| NSPEC                      | IS | R     | AT | 2                       |
| NSPEC                      | IS | R     | AT | 3                       |
| NSPEC                      | IS | R     | AT | 4                       |
| NSPEC                      | IS | R     | AT | 5                       |
| NSPEC                      | IS | R     | AT | 6                       |
| NSPEC                      | IS | C     | AT | 7                       |
| NSPEC                      | IS | C     | AT | 8                       |
| NSPEC                      | IS | C     | AT | 9                       |
| NSPEC                      | IS | C     | AT | 10                      |
| NSPEC                      | IS | C     | AT | 11                      |
| NSPEC                      | IS | C     | AT | 12                      |
| NSPEC                      | IS | C     | AT | 13                      |
| NSPEC                      | IS | C     | AT | 14                      |
| NSPEC                      | IS | C     | AT | 15                      |
| CONNECT                    | IS | E3    | RC | AT 10                   |
| DEFAULT MLEVEL IS ATOM     |    |       |    |                         |
| MLEVEL                     | IS | CLASS | AT | 7 8 9 10 11 12 13 14 15 |
| DEFAULT ECLEVEL IS LIMITED |    |       |    |                         |

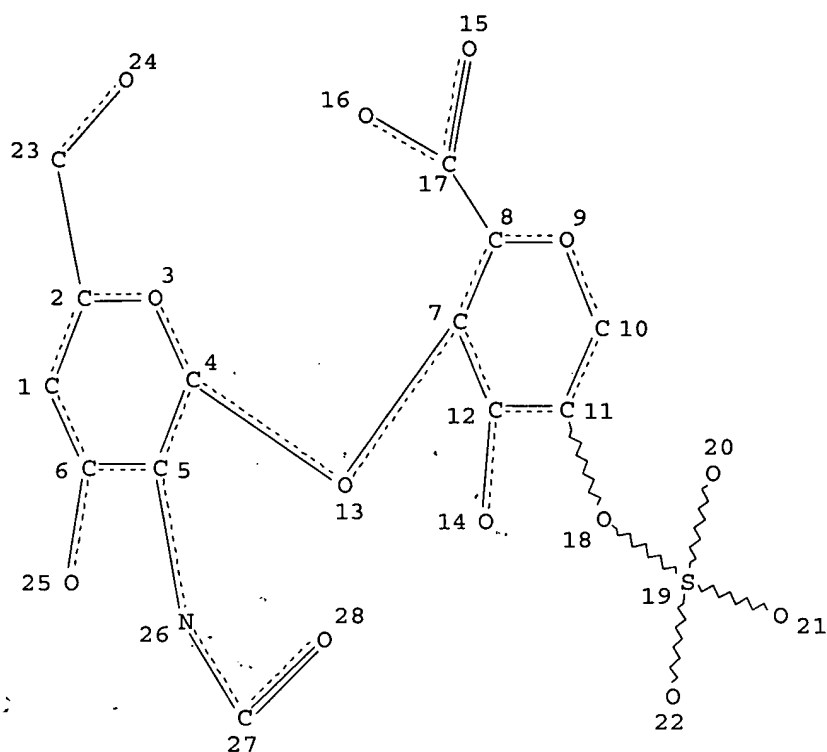
## GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 15

## STEREO ATTRIBUTES: NONE

L3 1062 SEA FILE=REGISTRY SSS FUL L1  
L18 STR





## NODE ATTRIBUTES:

|         |       |       |    |
|---------|-------|-------|----|
| NSPEC   | IS R  | AT    | 1  |
| NSPEC   | IS R  | AT    | 2  |
| NSPEC   | IS R  | AT    | 3  |
| NSPEC   | IS R  | AT    | 4  |
| NSPEC   | IS R  | AT    | 5  |
| NSPEC   | IS R  | AT    | 6  |
| NSPEC   | IS R  | AT    | 7  |
| NSPEC   | IS R  | AT    | 8  |
| NSPEC   | IS R  | AT    | 9  |
| NSPEC   | IS R  | AT    | 10 |
| NSPEC   | IS R  | AT    | 11 |
| NSPEC   | IS R  | AT    | 12 |
| NSPEC   | IS C  | AT    | 13 |
| NSPEC   | IS C  | AT    | 14 |
| NSPEC   | IS C  | AT    | 15 |
| NSPEC   | IS C  | AT    | 16 |
| NSPEC   | IS C  | AT    | 17 |
| NSPEC   | IS C  | AT    | 18 |
| NSPEC   | IS C  | AT    | 19 |
| NSPEC   | IS C  | AT    | 20 |
| NSPEC   | IS C  | AT    | 21 |
| NSPEC   | IS C  | AT    | 22 |
| NSPEC   | IS C  | AT    | 23 |
| NSPEC   | IS C  | AT    | 24 |
| NSPEC   | IS C  | AT    | 25 |
| NSPEC   | IS C  | AT    | 26 |
| NSPEC   | IS C  | AT    | 27 |
| NSPEC   | IS C  | AT    | 28 |
| CONNECT | IS E3 | RC AT | 17 |

DEFAULT MLEVEL IS ATOM  
MLEVEL IS CLASS AT 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE  
L20 79 SEA FILE=REGISTRY SUB=L3 SSS FUL L18

100.0% PROCESSED 199 ITERATIONS 79 ANSWERS  
SEARCH TIME: 00.00.01

=> d que nos L149

L1 STR  
L3 1062 SEA FILE=REGISTRY SSS FUL L1  
L18 STR  
L20 79 SEA FILE=REGISTRY SUB=L3 SSS FUL L18  
L148 79 SEA FILE=REGISTRY POLYLINK L20  
L149 0 SEA FILE=REGISTRY ABB=ON PLU=ON L148 NOT L20

*79 registry numbers have  
the 2 monomers  
attached to  
each other*

*query  
logic  
shows  
that L20=L148*

=> => => file caplus

FILE 'CAPLUS' ENTERED AT 15:30:55 ON 22 FEB 2006  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
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FILE COVERS 1907 - 22 Feb 2006 VOL 144 ISS 9  
FILE LAST UPDATED: 21 Feb 2006 (20060221/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>  
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d que nos L48

L46 422 SEA FILE=CAPLUS ABB=ON PLU=ON LINHARDT R?/AU  
L47 31492 SEA FILE=CAPLUS ABB=ON PLU=ON KIM Y?/AU  
L48 35 SEA FILE=CAPLUS ABB=ON PLU=ON L46 AND L47

*AUTHOR  
SEARCH  
(structure hits ~~with~~ or RNs  
will show if present)*

=> d que nos L49

```
L1          STR
L2          50 SEA FILE=REGISTRY SSS SAM L1
L3          1062 SEA FILE=REGISTRY SSS FUL L1
L18         STR
L20         79 SEA FILE=REGISTRY SUB=L3 SSS FUL L18
L21         33 SEA FILE=CAPLUS ABB=ON  PLU=ON  L20
L22         9 SEA FILE=CAPLUS ABB=ON  PLU=ON  L2 (L) (THU OR DMA OR PAC OR
          PKT OR BAC)/RL
L23         25 SEA FILE=CAPLUS ABB=ON  PLU=ON  ACHARAN SULFATE/OBI
L25         1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ACHARAN SULFATE/CN
L26         1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ACHARAN, N-DEACETYL-N-SULFO?/
          CN
L27         24 SEA FILE=CAPLUS ABB=ON  PLU=ON  L25
L28         5 SEA FILE=CAPLUS ABB=ON  PLU=ON  L26
L33         28 SEA FILE=CAPLUS ABB=ON  PLU=ON  ACHARAN?/BI
L36         28 SEA FILE=CAPLUS ABB=ON  PLU=ON  L33 OR L27 OR L28 OR L23
L46         422 SEA FILE=CAPLUS ABB=ON  PLU=ON  LINHARDT R?/AU
L47         31492 SEA FILE=CAPLUS ABB=ON  PLU=ON  KIM Y?/AU
L48         35 SEA FILE=CAPLUS ABB=ON  PLU=ON  L46 AND L47
L49         13 SEA FILE=CAPLUS ABB=ON  PLU=ON  L48 AND (L21 OR L22 OR L36)
```

=> s L48-L49

L161 35 (L48 OR L49)

=> file medline

FILE 'MEDLINE' ENTERED AT 15:30:58 ON 22 FEB 2006

FILE LAST UPDATED: 21 FEB 2006 (20060221/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 will soon be available. For details  
on the 2005 reload, enter HELP RLOAD at an arrow prompt (=>).  
See also:

<http://www.nlm.nih.gov/mesh/>  
[http://www.nlm.nih.gov/pubs/techbull/nd04/nd04\\_mesh.html](http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html)  
[http://www.nlm.nih.gov/pubs/techbull/nd05/nd05\\_med\\_data\\_changes.html](http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html)  
[http://www.nlm.nih.gov/pubs/techbull/nd05/nd05\\_2006\\_MeSH.html](http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html)

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the  
MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate

=> d que nos L75

```
L73         283 SEA FILE=MEDLINE ABB=ON  PLU=ON  LINHARDT R?/AU
L74         10317 SEA FILE=MEDLINE ABB=ON  PLU=ON  KIM Y?/AU
L75         31 SEA FILE=MEDLINE ABB=ON  PLU=ON  L73 AND L74
```

=> d que nos L76

```
L25         1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ACHARAN SULFATE/CN
```

```
L26      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ACHARAN, N-DEACETYL-N-SULFO?/  
          CN  
L50      18 SEA FILE=MEDLINE ABB=ON  PLU=ON  ACHARAN?  
L56      SEL  PLU=ON  L25 1- CHEM :      2 TERMS  
L57      18 SEA FILE=MEDLINE ABB=ON  PLU=ON  L56  
L58      SEL  PLU=ON  L26 1- CHEM :      2 TERMS  
L59      4 SEA FILE=MEDLINE ABB=ON  PLU=ON  L58  
L60      18 SEA FILE=MEDLINE ABB=ON  PLU=ON  L50 OR L57 OR L59  
L73      283 SEA FILE=MEDLINE ABB=ON  PLU=ON  LINHARDT R?/AU  
L74      10317 SEA FILE=MEDLINE ABB=ON  PLU=ON  KIM Y?/AU  
L75      31 SEA FILE=MEDLINE ABB=ON  PLU=ON  L73 AND L74  
L76      9 SEA FILE=MEDLINE ABB=ON  PLU=ON  L75 AND L60
```

=> s L75-L76

L162 31 (L75 OR L76)

=> file embase

FILE 'EMBASE' ENTERED AT 15:31:01 ON 22 FEB 2006  
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FILE COVERS 1974 TO 20 Feb 2006 (20060220/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

=> d que nos L99

```
L97      261 SEA FILE=EMBASE ABB=ON  PLU=ON  LINHARDT R?/AU  
L98      8968 SEA FILE=EMBASE ABB=ON  PLU=ON  KIM Y?/AU  
L99      21 SEA FILE=EMBASE ABB=ON  PLU=ON  L97 AND L98
```

=> d que nos L100

```
L25      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ACHARAN SULFATE/CN  
L26      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ACHARAN, N-DEACETYL-N-SULFO?/  
          CN  
L77      16 SEA FILE=EMBASE ABB=ON  PLU=ON  ACHARAN?  
L83      SEL  PLU=ON  L25 1- CHEM :      2 TERMS  
L84      16 SEA FILE=EMBASE ABB=ON  PLU=ON  L83  
L85      SEL  PLU=ON  L26 1- CHEM :      2 TERMS  
L86      4 SEA FILE=EMBASE ABB=ON  PLU=ON  L85  
L87      16 SEA FILE=EMBASE ABB=ON  PLU=ON  L77 OR L84 OR L86  
L88      851781 SEA FILE=EMBASE ABB=ON  PLU=ON  ?CANCER?  
L89      778474 SEA FILE=EMBASE ABB=ON  PLU=ON  ?TUMOR? OR ?TUMOUR?  
L90      90530 SEA FILE=EMBASE ABB=ON  PLU=ON  ?SARCOMA?  
L91      230147 SEA FILE=EMBASE ABB=ON  PLU=ON  ?NEOPLAS?  
L92      517907 SEA FILE=EMBASE ABB=ON  PLU=ON  ?CARCINO?  
L93      34532 SEA FILE=EMBASE ABB=ON  PLU=ON  ?ANGIOGEN?  
L94      1349056 SEA FILE=EMBASE ABB=ON  PLU=ON  NEOPLASM+NT/CT  
L95      4217 SEA FILE=EMBASE ABB=ON  PLU=ON  ANGIOGENESIS INHIBITOR/CT  
L96      4 SEA FILE=EMBASE ABB=ON  PLU=ON  L87 AND (L88 OR L89 OR L90 OR  
          L91 OR L92 OR L93 OR L94 OR L95)  
L97      261 SEA FILE=EMBASE ABB=ON  PLU=ON  LINHARDT R?/AU  
L98      8968 SEA FILE=EMBASE ABB=ON  PLU=ON  KIM Y?/AU
```

L99 21 SEA FILE=EMBASE ABB=ON PLU=ON L97 AND L98  
L100 7 SEA FILE=EMBASE ABB=ON PLU=ON L99 AND (L96 OR L87)

=> s L99-L100

L163 21 (L99 OR L100)

=> file biosis

FILE 'BIOSIS' ENTERED AT 15:31:04 ON 22 FEB 2006  
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FILE COVERS 1969 TO DATE.  
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT  
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 15 February 2006 (20060215/ED)

=> d que nos L122

L120 359 SEA FILE=BIOSIS ABB=ON PLU=ON LINHARDT R?/AU  
L121 15625 SEA FILE=BIOSIS ABB=ON PLU=ON KIM Y?/AU  
L122 40 SEA FILE=BIOSIS ABB=ON PLU=ON L120 AND L121

=> d que nos L123

L25 1 SEA FILE=REGISTRY ABB=ON PLU=ON ACHARAN SULFATE/CN  
L26 1 SEA FILE=REGISTRY ABB=ON PLU=ON ACHARAN, N-DEACETYL-N-SULFO?/  
CN  
L101 22 SEA FILE=BIOSIS ABB=ON PLU=ON ACHARAN?  
L103 17 SEA FILE=BIOSIS ABB=ON PLU=ON L25  
L104 1 SEA FILE=BIOSIS ABB=ON PLU=ON L26  
L107 SEL PLU=ON L25 1- CHEM : 2 TERMS  
L108 21 SEA FILE=BIOSIS ABB=ON PLU=ON L107  
L109 SEL PLU=ON L26 1- CHEM : 2 TERMS  
L110 4 SEA FILE=BIOSIS ABB=ON PLU=ON L109  
L111 22 SEA FILE=BIOSIS ABB=ON PLU=ON L101 OR L103 OR L104 OR L108  
OR L110  
L112 546518 SEA FILE=BIOSIS ABB=ON PLU=ON ?CANCER?  
L113 976062 SEA FILE=BIOSIS ABB=ON PLU=ON ?TUMOR? OR ?TUMOUR?  
L114 95426 SEA FILE=BIOSIS ABB=ON PLU=ON ?SARCOMA?  
L115 759144 SEA FILE=BIOSIS ABB=ON PLU=ON ?NEOPLAS?  
L116 507193 SEA FILE=BIOSIS ABB=ON PLU=ON ?CARCINO?  
L117 35893 SEA FILE=BIOSIS ABB=ON PLU=ON ?ANGIOGEN?  
L118 4 SEA FILE=BIOSIS ABB=ON PLU=ON L111 AND (L112 OR L113 OR L114  
OR L115 OR L116 OR L117)  
L120 359 SEA FILE=BIOSIS ABB=ON PLU=ON LINHARDT R?/AU  
L121 15625 SEA FILE=BIOSIS ABB=ON PLU=ON KIM Y?/AU  
L122 40 SEA FILE=BIOSIS ABB=ON PLU=ON L120 AND L121  
L123 11 SEA FILE=BIOSIS ABB=ON PLU=ON L122 AND (L111 OR L118)

=> s L122-L123

L164 40 (L122 OR L123)

=> file wpix

FILE 'WPIX' ENTERED AT 15:31:07 ON 22 FEB 2006  
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FILE LAST UPDATED: 17 FEB 2006 <20060217/UP>  
MOST RECENT DERWENT UPDATE: 200612 <200612/DW>  
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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PLEASE VISIT:  
[http://www.stn-international.de/training\\_center/patents/stn\\_guide.pdf](http://www.stn-international.de/training_center/patents/stn_guide.pdf) <<<

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FOR FURTHER DETAILS:  
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PLEASE CHECK:  
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[http://www.stn-international.de/stndatabases/details/ipc\\_reform.html](http://www.stn-international.de/stndatabases/details/ipc_reform.html) and  
<http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf> <<<

=> d que nos L155

|      |       |     |           |        |        |                |
|------|-------|-----|-----------|--------|--------|----------------|
| L153 | 28    | SEA | FILE=WPIX | ABB=ON | PLU=ON | LINHARDT R?/AU |
| L154 | 28293 | SEA | FILE=WPIX | ABB=ON | PLU=ON | KIM Y?/AU      |
| L155 | 2     | SEA | FILE=WPIX | ABB=ON | PLU=ON | L153 AND L154  |

=> d que nos L160

|      |       |     |           |        |        |                         |
|------|-------|-----|-----------|--------|--------|-------------------------|
| L18  |       | STR |           |        |        |                         |
| L151 | 1     | SEA | FILE=WPIX | SSS    | FUL    | L18                     |
| L152 | 1     | SEA | FILE=WPIX | ABB=ON | PLU=ON | L151/DCR                |
| L153 | 28    | SEA | FILE=WPIX | ABB=ON | PLU=ON | LINHARDT R?/AU          |
| L154 | 28293 | SEA | FILE=WPIX | ABB=ON | PLU=ON | KIM Y?/AU               |
| L155 | 2     | SEA | FILE=WPIX | ABB=ON | PLU=ON | L153 AND L154           |
| L156 | 5     | SEA | FILE=WPIX | ABB=ON | PLU=ON | ACHARAN?                |
| L160 | 2     | SEA | FILE=WPIX | ABB=ON | PLU=ON | L155 AND (L152 OR L156) |

=> s L155 or L160

L165 2 L155 OR L160

=> file uspatfull

FILE 'USPATFULL' ENTERED AT 15:31:11 ON 22 FEB 2006  
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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 21 Feb 2006 (20060221/PD)  
 FILE LAST UPDATED: 21 Feb 2006 (20060221/ED)  
 HIGHEST GRANTED PATENT NUMBER: US7003800  
 HIGHEST APPLICATION PUBLICATION NUMBER: US2006037120  
 CA INDEXING IS CURRENT THROUGH 21 Feb 2006 (20060221/UPCA)  
 ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 21 Feb 2006 (20060221/PD)  
 REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2005  
 USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2005

=> d que nos L146

L144 28 SEA FILE=USPATFULL ABB=ON PLU=ON LINHARDT R?/AU  
 L145 4380 SEA FILE=USPATFULL ABB=ON PLU=ON KIM Y?/AU  
 L146 2 SEA FILE=USPATFULL ABB=ON PLU=ON L144 AND L145

=> d que nos L147

L1 STR  
 L3 1062 SEA FILE=REGISTRY SSS FUL L1  
 L18 STR  
 L20 79 SEA FILE=REGISTRY SUB=L3 SSS FUL L18  
 L25 1 SEA FILE=REGISTRY ABB=ON PLU=ON ACHARAN SULFATE/CN  
 L26 1 SEA FILE=REGISTRY ABB=ON PLU=ON ACHARAN, N-DEACETYL-N-SULFO?/  
 CN  
 L124 1 SEA FILE=USPATFULL ABB=ON PLU=ON L20  
 L125 2 SEA FILE=USPATFULL ABB=ON PLU=ON L25  
 L126 1 SEA FILE=USPATFULL ABB=ON PLU=ON L26  
 L129 SEL PLU=ON L25 1- CHEM : 2 TERMS  
 L130 4 SEA FILE=USPATFULL ABB=ON PLU=ON L129  
 L131 SEL PLU=ON L26 1- CHEM : 2 TERMS  
 L132 1 SEA FILE=USPATFULL ABB=ON PLU=ON L131  
 L133 4 SEA FILE=USPATFULL ABB=ON PLU=ON ACHARAN?  
 L134 5 SEA FILE=USPATFULL ABB=ON PLU=ON L124 OR L125 OR L126 OR  
 L130 OR L132 OR L133  
 L135 120107 SEA FILE=USPATFULL ABB=ON PLU=ON ?CANCER?  
 L136 104777 SEA FILE=USPATFULL ABB=ON PLU=ON ?TUMOR?  
 L137 12054 SEA FILE=USPATFULL ABB=ON PLU=ON ?TUMOUR?  
 L138 34800 SEA FILE=USPATFULL ABB=ON PLU=ON ?SARCOMA?  
 L139 37564 SEA FILE=USPATFULL ABB=ON PLU=ON ?NEOPLAS?  
 L140 67199 SEA FILE=USPATFULL ABB=ON PLU=ON ?CARCINO?  
 L141 22227 SEA FILE=USPATFULL ABB=ON PLU=ON ?ANGIOGEN?  
 L142 4 SEA FILE=USPATFULL ABB=ON PLU=ON L134 AND (L135 OR L136 OR  
 L137 OR L138 OR L139 OR L140 OR L141)  
 L144 28 SEA FILE=USPATFULL ABB=ON PLU=ON LINHARDT R?/AU  
 L145 4380 SEA FILE=USPATFULL ABB=ON PLU=ON KIM Y?/AU  
 L146 2 SEA FILE=USPATFULL ABB=ON PLU=ON L144 AND L145  
 L147 2 SEA FILE=USPATFULL ABB=ON PLU=ON L146 AND L142

=> s L146 or L147

L166 2 L146 OR L147

=> => dup rem L161 L162 L163 L164 L165 L166  
 FILE 'CAPLUS' ENTERED AT 15:32:34 ON 22 FEB 2006  
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PROCESSING COMPLETED FOR L161

PROCESSING COMPLETED FOR L162

PROCESSING COMPLETED FOR L163

PROCESSING COMPLETED FOR L164

PROCESSING COMPLETED FOR L165

PROCESSING COMPLETED FOR L166

L167 47 DUP REM L161 L162 L163 L164 L165 L166 (84 DUPLICATES REMOVED)  
ANSWERS '1-35' FROM FILE CAPLUS  
ANSWERS '36-37' FROM FILE MEDLINE  
ANSWERS '38-46' FROM FILE BIOSIS  
ANSWER '47' FROM FILE USPATFULL

=> d ibib abs hitind hitstr L167 1-35; d iall L167 36-46; d ibib abs kwic hitstr  
L167 47

L167 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2005:87281 CAPLUS

DOCUMENT NUMBER: 142:193004

TITLE: Characterization of heparan sulfate from the  
unossified antler of Cervus elaphus

AUTHOR(S): Ha, Young Wan; Jeon, Byong Tae; Moon, Sang Ho; Toyoda,  
Hidenao; Toida, Toshihiko; Linhardt, Robert J.  
; Kim, Yeong Shik

CORPORATE SOURCE: Natural Products Research Institute, College of  
Pharmacy, Seoul National University, Seoul, 110-460,  
S. Korea

SOURCE: Carbohydrate Research (2005), 340(3), 411-416

CODEN: CRBRAT; ISSN: 0008-6215

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The antler is the most rapidly growing tissue in the animal kingdom.  
According to previous reports, antler glycosaminoglycans (GAGs) consist of  
all kinds GAGs except for heparan sulfate (HS). Chondroitin sulfate is  
the major antler GAG component comprising 88% of the total uronic acid  
content. In the current study, we have isolated HS from antler for the  
first time and characterized it based on both NMR spectroscopy and  
disaccharide composition anal. Antler GAGs were isolated by protease treatment  
and followed by cetylpyridinium chloride precipitation The sensitivity of  
antler  
GAGs to heparin lyase III showed that this sample contained heparan  
sulfate. After incubation of antler GAGs with chondroitin lyase ABC, the  
HS-containing fraction was recovered by ethanol precipitation The composition  
of HS  
disaccharides in this fraction was determined by its complete depolymn. with a



mixture of heparin lyase I, II, and III and anal. of the resulting disaccharides by the reversed-phase (RP) ion pairing-HPLC, monitored by the fluorescence detection using 2-cyanoacetamide as a post-column labeling reagent. Eight unsatd. disaccharides ( $\Delta$ UA-GlcNAc,  $\Delta$ UA-GlcNS,  $\Delta$ UA-GlcNAc6S,  $\Delta$ UA2S-GlcNAc,  $\Delta$ UA-GlcNS6S,  $\Delta$ UA2S-GlcNS,  $\Delta$ UA2S-GlcNAc6S,  $\Delta$ UA2S-GlcNS6S) were produced from antler HS by digestion with the mixture of heparin lyases. The total content of 2-O-sulfo disaccharide units in antler HS was higher than that of heparan sulfate from most other animal sources.

CC 6-4 (General Biochemistry)

Section cross-reference(s): 13

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L167 ANSWER 2 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2005:174300 CAPLUS

DOCUMENT NUMBER: 142:417327

TITLE: Quantitative analysis of chondroitin sulfate in raw materials, ophthalmic solutions, soft capsules, and liquid preparations

AUTHOR(S): Sim, Joon-Soo; Jun, Gyungjin; Toida, Toshihiko; Cho, So Yean; Choi, Don Woong; Chang, Seung-Yeup; Linhardt, Robert J.; Kim, Yeong Shik

CORPORATE SOURCE: Natural Products Research Institute, College of Pharmacy, Seoul National University, Seoul, 110-460, S. Korea

SOURCE: Journal of Chromatography, B: Analytical Technologies in the Biomedical and Life Sciences (2005), 818(2), 133-139

CODEN: JCBAAI; ISSN: 1570-0232

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors performed the quant. anal. of chondroitin sulfate (CS) obtained from raw materials and various pharmaceutical preps. To quantify CS content in raw materials and in an ophthalmic solution, each test sample and the authentic CS were 1st digested by chondroitinase ABC. The CS disaccharides produced were analyzed by strong anion-exchange high-performance liquid chromatog. (SAX-HPLC) and CS content was quantified by calculating the total peak areas of the disaccharides derived from a CS calibration curve. In the case of soft capsules, CS was 1st extracted with hexane followed by phenol-chloroform to remove oil and protein ingredients. The extracted CS samples were depolymd. by chondroitinase ABC and CS content was determined. Quant. anal. of the disaccharides derived from raw materials and an ophthalmic solution showed the CS contents (%) were 39.5 to 105.6 and 103.3, resp. In case of CS anal. in soft capsules and liquid preps., the overall recovery (%) of the spiked CS was 96.79 - 103.54 and 97.10 to 103.17, resp. In conclusion, the quant. anal. of the disaccharides produced by enzymic digestion can be used in the direct quantitation of CS containing pharmaceutical formulations.

CC 64-2 (Pharmaceutical Analysis)

Section cross-reference(s): 17, 63

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L167 ANSWER 3 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 2004:740132 CAPLUS

DOCUMENT NUMBER: 141:254539

TITLE: Antitumor inhibitors and use thereof

INVENTOR(S): Linhardt, Robert J.; Kim, Yeong Shik  
 PATENT ASSIGNEE(S): University of Iowa Research Foundation, USA  
 SOURCE: PCT Int. Appl., 28 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND  | DATE     | APPLICATION NO. | DATE       |
|---|---|----------|-----------------|------------|
| WO 2004075848   | A2  | 20040910 | WO 2004-US5402  | 20040223   |
| WO 2004075848   | A3  | 20050414 |                 |            |
| W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI<br>RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG |   |          |                 |            |
| US 2005075312   | A1  | 20050407 | US 2004-786613  | 20040223   |
| PRIORITY APPLN. INFO.:  |   |          | US 2003-449661P | P 20030224 |
| AB  | The present invention provides pharmaceutical compns. for the treatment of cancer and inhibiting an increase in the volume or mass of a tumor, and methods for the treatment of cancer and inhibiting an increase in the volume or mass of a tumor. |          |                 |            |
| IC  | ICM A61K  |          |                 |            |
| CC  | 1-6 (Pharmacology)  |          |                 |            |
| ST  | antitumor angiogenesis inhibitor <b>acharan sulfate</b> lung carcinoma  |          |                 |            |
| IT  | Angiogenesis inhibitors<br>Antitumor agents<br>Sarcoma<br>(antitumor angiogenesis inhibitor <b>acharan sulfate</b> )  |          |                 |            |
| IT  | Lung, neoplasm<br>(carcinoma; antitumor angiogenesis inhibitor <b>acharan sulfate</b> )   |          |                 |            |
| IT  | Cell proliferation<br>(inhibition, endothelial; antitumor angiogenesis inhibitor <b>acharan sulfate</b> )   |          |                 |            |
| IT  | Carcinoma<br>(pulmonary; antitumor angiogenesis inhibitor <b>acharan sulfate</b> )  |          |                 |            |
| IT  | <b>192662-57-0, Acharan sulfate</b><br>RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)<br>(I and II; antitumor angiogenesis inhibitor <b>acharan sulfate</b> )                                      |          |                 |            |
| IT  | <b>192662-57-0, Acharan sulfate</b><br>RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)<br>(I and II; antitumor angiogenesis inhibitor <b>acharan sulfate</b> )                                      |          |                 |            |
| RN  | 192662-57-0 CAPLUS  |          |                 |            |
| CN  | Acharan, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)   |          |                 |            |

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L167 ANSWER 4 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2004:304141 CAPLUS

DOCUMENT NUMBER: 140:385739

TITLE: Long duration of anticoagulant activity and protective effects of **acharan sulfate** in vivo

AUTHOR(S): Li, Da-Wei; Lee, In Sun; Sim, Joon-Soo; Toida, Toshihiko; **Linhardt, Robert J.; Kim, Yeong Shik**

CORPORATE SOURCE: College of Pharmacy, Natural Products Research Institute, Seoul National University, Seoul, 110-460, S. Korea

SOURCE: Thrombosis Research (2004), 113(1), 67-73

CODEN: THBRAA; ISSN: 0049-3848

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Introduction: We previously reported that a new glycosaminoglycan, **acharan sulfate** (AS) from the African giant snail *Achatina fulica* showed anticoagulant activity in vitro, but was much less active when compared to heparin. In the present study, the anticoagulant activity of AS was investigated in vivo. Methods: AS and heparin were administered to mice and rats in various doses and the anticoagulant activities were measured by aPTT assay. Both were also compared in a thrombin-induced lethality animal model. As one of the possible mechanisms, AS-thrombin interaction was studied by using surface plasmon resonance spectroscopy. Results: I.V. administration of AS to mice prolonged the clotting time (aPTT) in a time and dose-dependent manner. Although the anticoagulant activity was low in rats, it steadily increased over 5 h after administration of AS (30 mg/kg). In contrast, the increase in aPTT induced by 5 mg/kg of heparin was restored to a normal level after 3 h. In a thrombin-induced lethality model in mice, AS (20 mg/kg) protected against lethality by 80%, while heparin (20 mg/kg) did not show any protective activity beyond 3.5 h post-administration. AS could be also detected in plasma even 5 h after i.v. administration to rats. The binding constant (KD) of AS to thrombin was  $7.27 \times 10^{-6}$  M, corresponding to moderate binding affinity. Conclusions: These results show that the longer duration of AS in blood could prolong the clotting time determined by aPTT and offering protection against thrombin-induced lethality. One possible mechanism may result from AS-thrombin interaction.

CC 1-8 (Pharmacology)

ST anticoagulant **acharan sulfate** thrombin clotting time

IT Anticoagulants

Blood coagulation

(long duration of anticoagulant activity and protective effects of **acharan sulfate** in vivo)

IT 192662-57-0, **Acharan sulfate**

RL: ANT (Analyte); PAC (Pharmacological activity); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(long duration of anticoagulant activity and protective effects of **acharan sulfate** in vivo)

IT 9002-04-4, Thrombin

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(long duration of anticoagulant activity and protective effects of **acharan sulfate** in vivo)

IT 192662-57-0, **Acharan sulfate**

RL: ANT (Analyte); PAC (Pharmacological activity); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(long duration of anticoagulant activity and protective effects of  
**acharan sulfate** in vivo)

RN 192662-57-0 CAPLUS

CN Acharan, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L167 ANSWER 5 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 2004:15557 CAPLUS

DOCUMENT NUMBER: 140:412133

TITLE: Enhancement of heparin and heparin disaccharide  
absorption by the *Phytolacca americana* saponins

AUTHOR(S): Cho, So Yean; Sim, Joon-soo; Kang, Sam Sik; Jeong,  
Choon-sik; **Linhardt, Robert J.; Kim,  
Yeong Shik**

CORPORATE SOURCE: Natural Products Research Institute, College of  
Pharmacy, Seoul National University, Seoul, 110-460,  
S. Korea

SOURCE: Archives of Pharmacal Research (2003), 26(12),  
1102-1108

CODEN: APHRDQ; ISSN: 0253-6269

PUBLISHER: Pharmaceutical Society of Korea

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We studied the effects of phytolaccosides, saponins from *Phytolacca americana*, on the intestinal absorption of heparin in vitro and in vivo. The absorption enhancing activity of these compds. (phytolaccosides B, D2, E, F, G and I) was determined by changes in transepithelial elec. resistance (TEER) and the transport amount of heparin disaccharide, the major repeating unit of heparin, across Caco-2 cell monolayers. With the exception of phytolaccoside G, all of them decreased TEER values and increased the permeability in a dose-dependent and time-dependent manner. In vitro, phytolaccosides B, D2, and E showed significant absorption enhancing activities, while effects by phytolaccoside F and I were mild. In vivo, phytolaccoside E increased the activated partial thromboplastin time (APTT) and thrombin time, indicating that phytolaccoside E modulated the transport of heparin in intestinal route. These results suggest that a series of phytolaccosides from *Phytolacca americana* can be applied as pharmaceutical excipients to improve the permeability of macromols. and hydrophilic drugs having difficulty in absorption across the intestinal epithelium.

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 1

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L167 ANSWER 6 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 7

ACCESSION NUMBER: 2003:209472 CAPLUS

DOCUMENT NUMBER: 139:207217

TITLE: Suppression of tumor growth by a new glycosaminoglycan  
isolated from the African giant snail *Achatina fulica*

AUTHOR(S): Lee, Yeon Sil; Yang, Hyun Ok; Shin, Kuk Hyun; Choi,  
Hyung Seok; Jung, Sang Hoon; **Kim, Yong Man;**  
Oh, Deok Kun; **Linhardt, Robert J.; Kim,  
Yeong Shik**

CORPORATE SOURCE: College of Pharmacy, Natural Products Research  
Institute, Seoul National University, Seoul,  
Jongno-Ku, 110-460, S. Korea

SOURCE: European Journal of Pharmacology (2003), 465(1-2), 191-198  
CODEN: EJPHAZ; ISSN: 0014-2999  
PUBLISHER: Elsevier Science B.V.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB **Acharan** sulfate is a new type of glycosaminoglycan from the giant African snail, *Achatina fulica*. **Acharan** sulfate, which has a primary repeating disaccharide structure of  $\alpha$ -d-N-acetylglucosaminyl-2-O-sulfo- $\alpha$ -l-iduronic acid, was studied as a potential antitumor agent in both in vivo and in vitro assays. The antiangiogenic activity of **acharan** sulfate was evaluated in the chorioallantoic membrane assay and by measuring its effect on the proliferation of calf pulmonary artery endothelial cells. In vivo, a matrigel plug assay showed that **acharan** sulfate suppressed basic fibroblast growth factor (bFGF)-stimulated angiogenesis and lowered the Hb content inside the plug. **Acharan** sulfate was administered s.c. at two doses for 15 days to C57BL/6 mice implanted with murine Lewis lung carcinoma in the back. It was also administered i.p. to ICR mice bearing sarcoma 180 at a dose of 30 mg/kg. S.c. injection of **acharan** sulfate at doses of 10 and 30 mg/kg decreased tumor weight and tumor volume by 40% without toxicity or resistance. I.p. injection of **acharan** sulfate also decreased tumor weight and volume by 40% in sarcoma 180-bearing mice. These results suggest that the antitumor activity of **acharan** sulfate may be related to the inhibition of angiogenesis.  
CC 1-6 (Pharmacology)  
ST glycosaminoglycan **acharan sulfate** antitumor lung carcinoma sarcoma *Achatina* snail; angiogenesis inhibitor glycosaminoglycan **acharan sulfate** antitumor *Achatina* snail  
IT 192662-57-0, **Acharan sulfate**  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(suppression of tumor growth by a new glycosaminoglycan isolated from the African giant snail *Achatina fulica*)  
IT 192662-57-0, **Acharan sulfate**  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(suppression of tumor growth by a new glycosaminoglycan isolated from the African giant snail *Achatina fulica*)  
RN 192662-57-0 CAPLUS  
CN **Acharan**, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L167 ANSWER 7 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 8

ACCESSION NUMBER: 2002:210512 CAPLUS

DOCUMENT NUMBER: 137:87808

TITLE: Enhancement of paracellular transport of heparin disaccharide across Caco-2 cell monolayers

AUTHOR(S): Cho, So Yean; Kim, Jong Sik; Li, Hong; Shim, Changkoo; Linhardt, Robert J.; Kim, Yeong Shik

CORPORATE SOURCE: Natural Products Research Institute, Seoul National University, Seoul, 110-460, S. Korea

SOURCE: Archives of Pharmacal Research (2002), 25(1), 86-92

CODEN: APHRDQ; ISSN: 0253-6269

PUBLISHER: Pharmaceutical Society of Korea

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The enhancement of the paracellular transport of heparin disaccharide (the major repeating unit of heparin) across Caco-2 cell monolayers by various absorption enhancers was tested. The cytotoxicity of these enhancers was also examined. The effects of Quillaja saponin, dipotassium glycyrrhizinate, 18 $\beta$ -glycyrrhetinic acid, sodium caprate, Triton X-100, and taurine were determined by measuring changes in transepithelial elec. resistance (TEER) and the amount of heparin disaccharide transported. 18 $\beta$ -Glycyrrhetinic acid and taurine decreased TEER and increased the permeability to heparin disaccharide in a concentrate- and time-dependent manner with little or negligible cytotoxicity. The results indicate that these absorption enhancers can widen the tight junction, which is a dominant paracellular absorption route of hydrophilic compds. It is possible that these absorption enhancers could be used as pharmaceutical excipients to improve the transport of macromols. and hydrophilic drugs having low permeability across the intestinal epithelium.

CC 1-2 (Pharmacology)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L167 ANSWER 8 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 9

ACCESSION NUMBER: 2001:68553 CAPLUS

DOCUMENT NUMBER: 134:262794

TITLE: Active Site of Chondroitin AC Lyase Revealed by the Structure of Enzyme-Oligosaccharide Complexes and Mutagenesis

AUTHOR(S): Huang, Weijun; Boju, Lorena; Tkalec, Lydia; Su, Hongsheng; Yang, Hyun-Ok; Gunay, Nur Sibel; Linhardt, Robert J.; Kim, Yeong Shik; Matte, Allan; Cygler, Mirosław

CORPORATE SOURCE: Biotechnology Research Institute, Montreal, QC, H4P 2R2, Can.

SOURCE: Biochemistry (2001), 40(8), 2359-2372

PUBLISHER: CODEN: BICHAW; ISSN: 0006-2960

DOCUMENT TYPE: American Chemical Society

LANGUAGE: Journal

English

AB The crystal structures of Flavobacterium heparinium chondroitin AC lyase (chondroitinase AC; E.C. 4.2.2.5) bound to dermatan sulfate hexasaccharide (DSHexa), tetrasaccharide (DStetra), and hyaluronic acid tetrasaccharide (HATetra) have been refined at 2.0, 2.0, and 2.1 Å resolution, resp. The structure of the Tyr234Phe mutant of AC lyase bound to a chondroitin sulfate tetrasaccharide (CStetra) has also been determined to 2.3 Å resolution. For each of these complexes, four (DSHexa and CStetra) or two (DStetra and HATetra) ordered sugars are visible in electron d. maps. The lyase AC DSHexa and CStetra complexes reveal binding at four subsites, -2, -1, +1, and +2, within a narrow and shallow protein channel. We suggest that subsites -2 and -1 together represent the substrate recognition area, +1 is the catalytic subsite and +1 and +2 together represent the product release area. The putative catalytic site is located between the substrate recognition area and the product release area, carrying out catalysis at the +1 subsite. Four residues near the catalytic site, His225, Tyr234, Arg288, and Glu371 together form a catalytic tetrad. The mutations His225Ala, Tyr234Phe, Arg288Ala, and Arg292Ala, revealed residual activity for only the Arg292Ala mutant. Structural data indicate that Arg292 is primarily involved in recognition of the N-acetyl and sulfate moieties of galactosamine, but does not participate directly in catalysis. Candidates for the general base, removing the proton attached to C-5 of the glucuronic acid at the +1 subsite, are Tyr234, which could be transiently deprotonated during catalysis, or His225. Tyrosine 234 is a candidate to protonate the leaving group. Arginine 288 likely

contributes to charge neutralization and stabilization of the enolate anion intermediate during catalysis.

CC 7-5 (Enzymes)

Section cross-reference(s): 75

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L167 ANSWER 9 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 10

ACCESSION NUMBER: 2001:820002 CAPLUS

DOCUMENT NUMBER: 136:99401

TITLE: Localization and characterization of **acharan sulfate** in the body of the giant African snail *Achatina fulica*

AUTHOR(S): Jeong, Jia; Toida, Toshihiko; Muneta, Yuki; Kosiishi, Ichiro; Imanari, Toshio; Linhardt, Robert J.; Choi, Hyung Seok; Wu, Song Ji; Kim, Yeong Shik

CORPORATE SOURCE: Natural Products Research Institute, Seoul National University, Seoul, 110-460, S. Korea

SOURCE: Comparative Biochemistry and Physiology, Part B: Biochemistry & Molecular Biology (2001), 130B(4), 513-519

CODEN: CBPBB8; ISSN: 1096-4959

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Acharan** sulfate is a glycosaminoglycan (GAG), having the structure  $\rightarrow 4$ -2-acetamido-2-deoxy- $\alpha$ -D-glucopyranose(1 $\rightarrow$ 4)-2-sulfo- $\alpha$ -L-idopyranosyluronic acid 1 $\rightarrow$ , isolated from the body of the giant African snail *Achatina fulica*. This GAG represents 3-5% of the dry weight of this snail's soft body tissues. Frozen sections and polyester wax sections of the snail's body were stained by Alcian blue-periodic acid-Schiff's reagent (PAS) to localize **acharan** sulfate. Alcian blue staining indicated that GAG was mainly secreted into the outer surface of the body from internal granules. A highly mucous material was collected and treated and the **acharan** sulfate was recovered by ethanol and cetyl pyridinium chloride precipitation. Crude **acharan** sulfate was purified by DEAE-Sephacel ion-exchange chromatog. Depolymn. of intact mucus and purified **acharan** sulfate fractions by heparin lyase II (heparitinase I) from *Flavobacterium heparinum* produced an unsatd. disaccharide as a major product, establishing the repeating unit of **acharan** sulfate. These results demonstrate that mucus in the granule and secreted to the outside of the body is composed entirely of **acharan** sulfate.

CC 12-1 (Nonmammalian Biochemistry)

ST snail **acharan sulfate**

IT *Achatina fulica*

Mucus

(localization and characterization of **acharan sulfate** in the body of the giant African snail *Achatina fulica*)

IT 192662-57-0, **Acharan sulfate**

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(localization and characterization of **acharan sulfate** in the body of the giant African snail *Achatina fulica*)

IT 192662-57-0, **Acharan sulfate**

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(localization and characterization of **acharan sulfate** in the body of the giant African snail *Achatina fulica*)

RN 192662-57-0 CAPLUS

CN **Acharan, hydrogen sulfate (ester)** (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L167 ANSWER 10 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 11

ACCESSION NUMBER: 2001:453852 CAPLUS

DOCUMENT NUMBER: 135:179758

TITLE: Enzymatic preparation of heparin disaccharides as  
building blocks in glycosaminoglycan synthesis

AUTHOR(S): Kim, Yeong Shik; Thanawiroon, Charuwan;  
Bazin, Helene G.; Kerns, Robert J.; Linhardt,  
Robert J.

CORPORATE SOURCE: Natural Products Research Institute, Seoul National  
University, Seoul, 110-460, S. Korea

SOURCE: Preparative Biochemistry & Biotechnology (2001),  
31(2), 113-124

CODEN: PBBIF4; ISSN: 1082-6068

PUBLISHER: Marcel Dekker, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 135:179758

AB Pharmaceutical heparin and heparan sulfate, isolated from a side-stream of  
a com. heparin manufacturing process, have been enzymically depolymd. with  
heparin lyases obtained from Flavobacterium heparinum. Heparin afforded a  
trisulfated disaccharide product that was recovered from the reaction  
mixture using gel permeation chromatog. Heparan sulfate afforded unsulfated  
disaccharide that was conveniently recovered from the product mixture by ion  
exchange chromatog. Both disaccharides were obtained in gram amts. at 90%  
or higher purity. Both enzymically prepared disaccharides were chemical  
protected to prepare building blocks required for the future chemical synthesis  
of therapeutically valuable heparin oligosaccharides.

CC 16-2 (Fermentation and Bioindustrial Chemistry)

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L167 ANSWER 11 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 12

ACCESSION NUMBER: 2000:121629 CAPLUS

DOCUMENT NUMBER: 132:161252

TITLE: N-acetylglucosamine-2-O-sulfated uronic acid compounds  
for angiogenesis inhibitors, and therapeutic use  
thereof

INVENTOR(S): Bernfield, Merton; Kim, Yeong Shik;  
Linhardt, Robert J.

PATENT ASSIGNEE(S): Children's Medical Center Corp, USA; The University of  
Iowa Research Foundation

SOURCE: U.S., 11 pp.  
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE     |
|------------------------|------|----------|-----------------|----------|
| US 6028061             | A    | 20000222 | US 1998-99296   | 19980618 |
| PRIORITY APPLN. INFO.: |      |          | US 1998-99296   | 19980618 |

AB A mol. having as its major repeating units N-acetylglucosamine alternating  
in sequence with 2-O-sulfated uronic acid inhibits FGF mitogenicity, and  
thus is useful in inhibiting angiogenesis. Addnl., the mol. has low



toxicity and inhibits FGF mitogenicity without affecting anticoagulant activity. One preferred mol. is a glycosaminoglycan, e.g. **acharan sulfate**. The mols. are in pharmaceutical compns. that can be used in the treatment of diseases which are angiogenesis-dependent.

IC ICM A61K031-715

ICS C07H013-12

INCL 514054000

CC 1-8 (Pharmacology)

Section cross-reference(s): 33, 63

ST angiogenesis inhibition acetylglucosamine sulfated uronate compd;  
glycosaminoglycan angiogenesis inhibition; **acharan sulfate** angiogenesis inhibition

IT 192662-56-9P, N-Sulfoacharan sulfate

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)

(acetylglucosamine-sulfated uronate compds. for angiogenesis inhibitors, and therapeutic use)

IT 192662-57-0, **Acharan sulfate**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(acetylglucosamine-sulfated uronate compds. for angiogenesis inhibitors, and therapeutic use)

IT 192662-56-9P, N-Sulfoacharan sulfate

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)

(acetylglucosamine-sulfated uronate compds. for angiogenesis inhibitors, and therapeutic use)

RN 192662-56-9 CAPLUS

CN Acharan, N-deacetyl-N-sulfo, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 192662-57-0, **Acharan sulfate**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(acetylglucosamine-sulfated uronate compds. for angiogenesis inhibitors, and therapeutic use)

RN 192662-57-0 CAPLUS

CN Acharan, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 4 . THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L167 ANSWER 12 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 13

ACCESSION NUMBER: 2000:757505 CAPLUS

DOCUMENT NUMBER: 134:56899

TITLE: Preparation and structural determination of dermatan sulfate-derived oligosaccharides

AUTHOR(S): Yang, Hyun Ok; Gunay, Nur Sibel; Toida, Toshihiko; Kuberan, Balagurunathan; Yu, Guangli; Kim, Yeong Shik; Linhardt, Robert J.

CORPORATE SOURCE: Department of Chemistry, Division of Medicinal and Natural Products Chemistry and Department of Chemical

and Biochemical Engineering, University of Iowa, Iowa  
City, IA, 52242, USA  
SOURCE: Glycobiology (2000), 10(10), 1033-1040  
CODEN: GLYCE3; ISSN: 0959-6658  
PUBLISHER: Oxford University Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Eight oligosaccharides were prepared from dermatan sulfate (DS) and their structures were elucidated. Porcine intestinal mucosal DS was subjected to controlled depolymn. using chondroitin ABC lyase (chondroitinase ABC). The oligosaccharide mixture formed was fractionated by low-pressure gel permeation chromatog. (GPC). Size uniform mixts. of disaccharides, tetrasaccharides, hexasaccharides, octasaccharides, decasaccharides, and dodecasaccharides were obtained. Each size-fractionated mixture was then purified on the basis of charge by repetitive semi-preparative strong-anion-exchange (SAX) high-performance liquid chromatog. (HPLC). This approach has led to the isolation of six homogeneous oligosaccharides. The size of the oligosaccharides were determined using GPC-HPLC. Treatment of tetrasaccharide and hexasaccharide fragments with Hg(OAc)<sub>2</sub> afforded trisaccharide and pentasaccharide products, resp. The purity of the oligosaccharides obtained was confirmed by anal. SAX-HPLC, and capillary electrophoresis (CE). The mol. mass and degree of sulfation of the eight purified oligosaccharides were elucidated using electrospray ionization (ESI) mass spectrometry and their structures were established with high field NMR (NMR) spectroscopy. These DS-oligosaccharides are currently being used to study for interaction of the DS with biol. important proteins.

CC 33-8 (Carbohydrates)

Section cross-reference(s): 7, 9, 22

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L167 ANSWER 13 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 14

ACCESSION NUMBER: 2000:583737 CAPLUS

DOCUMENT NUMBER: 133:146678

TITLE: Purification and characterization of a novel  
heparinase from Bacteroides stercoris HJ-15  
AUTHOR(S): Kim, Byung-Taek; Kim, Wan-Seok; Kim, Yeong  
Shik; Linhardt, Robert J.; Kim,  
Dong-Hyun

CORPORATE SOURCE: College of Pharmacy, Kyung Hee University, Seoul,  
130-701, S. Korea

SOURCE: Journal of Biochemistry (Tokyo) (2000), 128(2),  
323-328

CODEN: JOBIAO; ISSN: 0021-924X

PUBLISHER: Japanese Biochemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A novel type of heparinase (heparin lyase) (I) was purified from B. stercoris HJ-15, isolated from human intestine, which produced 3 kinds of heparinases. I was purified to apparent homogeneity by a combination of QAE-cellulose, DEAE-cellulose, CM-Sephadex C-50, hydroxylapatite, and HiTrap SP chromatogs. with a final specific activity of 19.5  $\mu\text{mol}/\text{min}/\text{mg}$ . I showed optimal activity at pH 7.2 and 45°, and the presence of 300 mM KCl greatly enhanced its activity. Purified I was inhibited by Cu<sup>2+</sup>, Pb<sup>2+</sup>, and some agents that modified His and Cys residues, and activated by reducing agents such as dithiothreitol and 2-mercaptoethanol. Purified Bacteroides I was an eliminase that showed its greatest activity on bovine intestinal heparan sulfate, and to a lesser extent on porcine intestinal heparan sulfate and heparin. I did

not act on **acharan** sulfate, but de-O-sulfated **acharan** sulfate and N-sulfoacharan sulfate were found to be poor substrates. The substrate specificity of I was similar to that of Flavobacterium heparinase II. However, an internal amino acid sequence of purified Bacteroides I showed significant (73%) homol. to Flavobacterium heparinase III and only 43% homol. to Flavobacterium heparinase II. These findings suggest that the Bacteroides I is a novel enzyme degrading glycosaminoglycans.

CC 7-2 (Enzymes)

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L167 ANSWER 14 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 15

ACCESSION NUMBER: 1999:792899 CAPLUS

DOCUMENT NUMBER: 132:204768

TITLE: Crystal Structure of Chondroitinase B from Flavobacterium heparinum and its Complex with a Disaccharide Product at 1.7 Å Resolution

AUTHOR(S): Huang, Weijun; Matte, Allan; Li, Yunge; Kim, Yeong Shik; Linhardt, Robert J.; Su, Hongsheng; Cygler, Mirosław

CORPORATE SOURCE: Biotechnology Research Institute, Montreal, QC, H4P 2R2, Can.

SOURCE: Journal of Molecular Biology (1999), 294(5), 1257-1269  
CODEN: JMOBAK; ISSN: 0022-2836

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Glycosaminoglycans (GAGs) are a family of acidic heteropolysaccharides, including such mols. as chondroitin sulfate, dermatan sulfate, heparin and keratan sulfate. Cleavage of the O-glycosidic bond within GAGs can be accomplished by hydrolases as well as lyases, yielding disaccharide and oligosaccharide products. We have determined the crystal structure of chondroitinase B, a glycosaminoglycan lyase from Flavobacterium heparinum, as well as its complex with a dermatan sulfate disaccharide product, both at 1.7 Å resolution. Chondroitinase B adopts the right-handed parallel β-helix fold, found originally in pectate lyase and subsequently in several polysaccharide lyases and hydrolases. Sequence homol. between chondroitinase B and a mannuronate lyase from Pseudomonas sp. suggests this protein also adopts the β-helix fold. Binding of the disaccharide product occurs within a pos. charged cleft formed by loops extending from the surface of the β-helix. Amino acid residues responsible for recognition of the disaccharide, as well as potential catalytic residues, have been identified. Two arginine residues, Arg318 and Arg364, are found to interact with the sulfate group attached to O-4 of N-acetylgalactosamine. Cleavage of dermatan sulfate likely occurs at the reducing end of the disaccharide, with Glu333 possibly acting as the general base. (c) 1999 Academic Press.

CC 7-5 (Enzymes)

Section cross-reference(s): 75

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L167 ANSWER 15 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 16

ACCESSION NUMBER: 1999:804912 CAPLUS

DOCUMENT NUMBER: 132:105537

TITLE: A new sulfated β-galactan from clams with anti-HIV activity

AUTHOR(S): Amornrut, Chaidedgumjorn; Toida, Toshihiko; Imanari, Toshio; Woo, Eun-Rhan; Park, Hokoon; Linhardt,

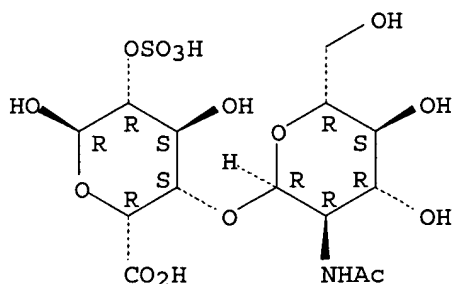
**Robert; Wu, Song Ji; Kim, Yeong Shik**  
 CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Chiba University,  
 Chiba, 263-8522, Japan  
 SOURCE: Carbohydrate Research (1999), 321(1-2), 121-127  
 CODEN: CRBRAT; ISSN: 0008-6215  
 PUBLISHER: Elsevier Science Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB A new polysaccharide composed of galactan sulfate with a  
 $\beta$ -(1 $\rightarrow$ 3)-glycosidic linkage has been isolated from the marine  
 clam species *Meretrix petechialis*. The polysaccharide was homogeneous in  
 its composition containing D-galactose. The glycosidic linkage was examined  
 by 2D DQF-COSY and 2D NOESY spectroscopy. The coupling constant of anomeric  
 proton was 7.8 Hz, suggesting a  $\beta$ -galacto configuration. The  
 downfield shift of H-2 of galactose residue demonstrated the presence of  
 2-O-sulfonate group. TQF-COSY confirmed that the C-6 position was  
 substituted with a sulfonate group. The anti-HIV activity of the  
 polysaccharides has been evaluated by the inhibition of syncytia  
 formation. The fusion index and percentage fusion inhibition of sulfated  
 galactan were 0.34 and 56% at 200  $\mu$ g/mL.  
 CC 12-1 (Nonmammalian Biochemistry)  
 Section cross-reference(s): 1, 33  
 REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L167 ANSWER 16 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 17  
 ACCESSION NUMBER: 1998:567562 CAPLUS  
 DOCUMENT NUMBER: 129:276176  
 TITLE: Determination of the structure of oligosaccharides  
 prepared from **acharan sulfate**  
 AUTHOR(S): **Kim, Yeong Shik**; Ahn, Mi Young; Wu, Song Ji;  
 Kim, Dong-Hyun; Toida, Toshihiko; Teesch, Lynn M.;  
 Park, Youmie; Yu, Guyong; Lin, Jihon; **Linhardt,**  
**Robert J.**  
 CORPORATE SOURCE: Natural Products Research Institute, Seoul National  
 University, Seoul, 110-460, S. Korea  
 SOURCE: Glycobiology (1998), 8(9), 869-877  
 CODEN: GLYCE3; ISSN: 0959-6658  
 PUBLISHER: Oxford University Press  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The fine structure of **acharan** sulfate, a recently discovered  
 glycosaminoglycan isolated from *Achatina fulica*, was examined This  
 glycosaminoglycan has a major disaccharide repeating unit of  
 $\rightarrow$ 4)- $\alpha$ -D-GlcNpAc(1 $\rightarrow$ 4)- $\alpha$ -L-IdoAp2S(1 $\rightarrow$   
 (where GlcNpAc is N-acetylglucosamine, IdoAp is iduronic acid, and S is  
 sulfate) making it structurally related to both heparin and heparan  
 sulfate. Using heparin lyases prepared from *Flavobacterium heparinum* and a  
 newly isolated heparinase from *Bacteroides stercoris*, the controlled  
 enzymic depolymn. of **acharan** sulfate was undertaken to prepare a  
 mixture of oligosaccharides. Fractionation of this mixture of  
 oligosaccharides by strong-anion-exchange high performance liquid chromatog.  
 afforded oligosaccharides that capillary electrophoresis established were  
 sufficiently pure for structural characterization. Electro-spray  
 ionization mass spectrometry identified two series of oligosaccharides,  
 one derived from **acharan** sulfate's major repeating unit and a  
 second minor group of under-sulfated oligosaccharides. Proton NMR  
 spectroscopy established the structure of these two classes of  
 oligosaccharides to be  $\Delta$ UAp2S(1 $\rightarrow$ 4)- $\alpha$ -D-

GlcNpAc (1→4) -α-L-IdoAp2S (1→]n4) -D-GlcNpAcα,β (where n = 0,1,2,3 and ΔUAp is 4-deoxy-α-L-threo-hex-4-enopyranosyluronic acid) and ΔUAp (1→[4) -α-D-GlcNpAc (1→4) -α-L-IdoAp2S (1→]m-D-GlcNpAcα,β (where m = 1,2,3). These results suggest the presence of minor sequence variants in **acharan sulfate** containing unsulfated iduronic acid having the structure →4) -α-D-GlcNpAc- (1→4) -α-L-IdoAp (1→.

- CC 33-8 (Carbohydrates)  
 Section cross-reference(s): 12  
 ST **acharan sulfate** glycosaminoglycan repeating unit;  
 Achatina fulica polysaccharide mol structure  
 IT Molecular structure  
 (structure of oligosaccharides prepared from **acharan sulfate**)  
 IT Glycosaminoglycans, miscellaneous  
 RL: MSC (Miscellaneous)  
 (structure of oligosaccharides prepared from **acharan sulfate**)  
 IT Achatina fulica  
 (structure of oligosaccharides prepared from **acharan sulfate** from)  
 IT 177791-14-9P  
 RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)  
 (repeating unit of **acharan sulfate** isolated from Achatina fulica)  
 IT 192662-57-0, **Acharan sulfate**  
 RL: MSC (Miscellaneous)  
 (structure of oligosaccharides prepared from by enzymic depolymn.)  
 IT 177791-14-9P  
 RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)  
 (repeating unit of **acharan sulfate** isolated from Achatina fulica)  
 RN 177791-14-9 CAPLUS  
 CN α-L-Idopyranuronic acid, 4-O-[2-(acetylamino)-2-deoxy-α-D-glucopyranosyl]-, 2-(hydrogen sulfate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



- IT 192662-57-0, **Acharan sulfate**  
 RL: MSC (Miscellaneous)  
 (structure of oligosaccharides prepared from by enzymic depolymn.)  
 RN 192662-57-0 CAPLUS  
 CN Acharan, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L167 ANSWER 17 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 18

ACCESSION NUMBER: 1998:503220 CAPLUS

DOCUMENT NUMBER: 129:200293

TITLE: Characterization of a Bacteroides species from human  
intestine that degrades glycosaminoglycans

AUTHOR(S): Ahn, Mi Young; Shin, Kuk Hyun; Kim, Dong-Hyun; Jung,  
Eun-Ah; Toida, Toshihiko; Linhardt, Robert J.  
; Kim, Yeong Shik

CORPORATE SOURCE: Natural Products Research Institute, Seoul National  
University, Seoul, 110-460, S. Korea

SOURCE: Canadian Journal of Microbiology (1998), 44(5),  
423-429

CODEN: CJMIAZ; ISSN: 0008-4166

PUBLISHER: National Research Council of Canada

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Polysaccharide lyases that can degrade glycosaminoglycans (GAGs) were  
identified in an anaerobic strain living in the human intestine. The  
strain was isolated from the stool of a healthy male and identified as  
Bacteroides sp. strain HJ-15. A detailed taxonomical study indicated the  
species is a strain of Bacteroides stercoris. The isolate was cultured  
and the polysaccharide lyase activity was partially purified. This enzyme  
preparation could act on GAGs containing either glucosamine or galactosamine,  
suggesting the presence of both heparinases and chondroitinases. Various  
GAGs were incubated with the partially purified enzyme and the products  
formed were analyzed by strong anion-exchange high performance liquid  
chromatog. and proton NMR spectroscopy. These studies demonstrated the  
presence of at least two types of polysaccharide lyases: heparin lyase and  
chondroitin sulfate lyase. The eliminative mechanism of these lyase  
enzymes was confirmed through the isolation of unsatd. disaccharide  
products. The heparin lyase acted on both heparin and **acharan**  
sulfate, a GAG recently isolated from Achatina fulica. The Bacteroides  
chondroitin lyase acted on chondroitin sulfates A, B (dermatan sulfate),  
and C, resembling chondroitin lyase ABC. The presence of a GAG-degrading  
organism in human intestine may pose problems for the effective oral  
administration of GAG drugs.

CC 10-2 (Microbial, Algal, and Fungal Biochemistry)

Section cross-reference(s): 7

IT 9005-49-6, Heparin, biological studies 24967-93-9, Chondroitin sulfate A  
24967-94-0, Chondroitin sulfate B 25322-46-7, Chondroitin sulfate C

**192662-57-0, Acharan sulfate**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
(Biological study); PROC (Process)

(characterization of a Bacteroides species from human intestine that  
degrades glycosaminoglycans)

IT **192662-57-0, Acharan sulfate**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
(Biological study); PROC (Process)

(characterization of a Bacteroides species from human intestine that  
degrades glycosaminoglycans)

RN 192662-57-0 CAPLUS

CN Acharan, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L167 ANSWER 18 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 19

ACCESSION NUMBER: 1998:798038 CAPLUS

DOCUMENT NUMBER: 130:162744

TITLE: Chemical sulfonation and anticoagulant activity of  
**acharan sulfate**AUTHOR(S): Wu, Song Ji; Chun, Moon Woo; Shin, Kuk Hyun; Toida,  
Toshihiko; Park, Youmie; **Linhardt, Robert J.**  
; **Kim, Yeong Shik**CORPORATE SOURCE: Natural Products Research Institute, Seoul National  
University, Seoul, 110-460, S. Korea

SOURCE: Thrombosis Research (1998), 92(6), 273-281

CODEN: THBRAA; ISSN: 0049-3848

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Acharan** sulfate is a glycosaminoglycan prepared from the giant African snail, *Achatina fulica*. This polysaccharide has a repeating disaccharide structure of  $\rightarrow 4$ )-2-deoxy-2-acetamido- $\alpha$ -D-glucopyranose (1 $\rightarrow$ 4)-2-sulfo- $\alpha$ -L-idopyranosyluronic acid (1 $\rightarrow$ ). Its structure is related to heparin and heparan sulfate but is distinctly different from all known members of these classes of glycosaminoglycans. Because of its structural similarities to heparin, chemical modified **acharan** sulfate was studied to understand the chemical structure effected its anticoagulant activity. After de-N-acetylation, **acharan** sulfate was N-sulfonated using either chlorosulfonic acid-pyridine or sulfur trioxide-trimeth-ylamine complex. The sulfate level in these products ranged from 22 to 24%(weight/weight), significantly less than that of heparin at 36%. The mol. weight of both N-sulfoacharan sulfates were comparable with that of heparin. In vitro anticoagulant activity assays showed that N-sulfoacharan sulfate derivs. were moderately active for the inhibition of thrombin and neither product showed any measurable anti-factor Xa activity. The differences in the activities of N-sulfoacharan sulfates produced by these two methods are probably ascribable to a small level of concomitant O-sulfonation obtained when using chlorosulfonic acid-pyridine.

CC 1-3 (Pharmacology)

ST sulfonation **acharan sulfate** glycosaminoglycan thrombin  
inhibiting structure; sulfoacharan sulfate deriv anticoagulant heparin  
structure; factor Xa sulfoacharan sulfate anticoagulant MSBARIT *Achatina fulica*

Anticoagulants

Sulfonation

(chemical sulfonation and anticoagulant activity of **acharan sulfate**)

IT Glycosaminoglycans, biological studies

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

(chemical sulfonation and anticoagulant activity of **acharan sulfate**)

IT Structure-activity relationship

(thrombin-inhibiting; chemical sulfonation and anticoagulant activity of **acharan sulfate**)

IT 192662-56-9D, N-Sulfoacharan sulfate, derivs.

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(chemical sulfonation and anticoagulant activity of **acharan sulfate**)

IT 9002-05-5, Factor Xa

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)  
(chemical sulfonation and anticoagulant activity of **acharan sulfate**)

IT 192662-57-0, **Acharan sulfate**  
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)  
(chemical sulfonation and anticoagulant activity of **acharan sulfate**)

IT 9005-49-6, Heparin, biological studies 9050-30-0, Heparan sulfate  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(chemical sulfonation and anticoagulant activity of **acharan sulfate**)

IT 192662-56-9D, N-Sulfoacharan sulfate, derivs.  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(chemical sulfonation and anticoagulant activity of **acharan sulfate**)

RN 192662-56-9 CAPLUS

CN Acharan, N-deacetyl-N-sulfo, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 192662-57-0, **Acharan sulfate**  
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)  
(chemical sulfonation and anticoagulant activity of **acharan sulfate**)

RN 192662-57-0 CAPLUS

CN Acharan, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L167 ANSWER 19 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 20

ACCESSION NUMBER: 1997:410216 CAPLUS

DOCUMENT NUMBER: 127:117569

TITLE: Glycosaminoglycans can influence fibroblast growth factor-2 mitogenicity without significant growth factor binding

AUTHOR(S): Wang, Huiming; Toida, Toshihiko; Kim, Yeong Shik; Capila, Ishan; Hileman, Ronald E.; Bernfield, Merton; Linhardt, Robert J.

CORPORATE SOURCE: Department of Pediatrics, Harvard Medical School, Boston, MA, 02115, USA

SOURCE: Biochemical and Biophysical Research Communications (1997), 235(2), 369-373

CODEN: BBRC9; ISSN: 0006-291X

PUBLISHER: Academic

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Fibroblast growth factors are important heparin binding, mitogenic proteins. The binding site in heparin and heparan sulfate for fibroblast growth factor-2 (basic fibroblast growth factor) has been described as rich in glucosamine-2-sulfate 1→4 linked to iduronic acid-2-sulfate. The glucosamine residue in the heparin binding site is also 6-sulfated. A new glycosaminoglycan, **acharan sulfate**, has been chemical modified to prepare a polysaccharide, N-sulfoacharan sulfate, consisting of glucosamine-2-sulfate 1→4 linked to iduronic acid-2-sulfate. **Acharan sulfate** binds very weakly to fibroblast



growth factor-2 while N-sulfoacharan sulfate binds with nearly the same affinity as heparin. Mitogenicity studies were performed using heparan sulfate-free cells stably transfected with fibroblast growth factor receptor-1. Acharan sulfate inhibits heparin's enhancement of fibroblast growth factor-2 mitogenic activity, without affecting cell viability, while N-sulfoacharan sulfate shows heparin-like activity but at a greatly reduced level. These results suggest addnl. mechanisms not requiring high affinity glycosaminoglycan binding to fibroblast growth factor-2 may be important in its mitogenic activity.

CC 2-5 (Mammalian Hormones)

IT 9005-49-6, Heparin, biological studies 106096-93-9, Basic fibroblast growth factor 192662-56-9, N-Sulfoacharan sulfate 192662-57-0, Acharan sulfate

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(glycosaminoglycans influence FGF-2 mitogenicity without growth factor binding)

IT 192662-56-9, N-Sulfoacharan sulfate 192662-57-0, Acharan sulfate

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(glycosaminoglycans influence FGF-2 mitogenicity without growth factor binding)

RN 192662-56-9 CAPLUS

CN Acharan, N-deacetyl-N-sulfo, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 192662-57-0 CAPLUS

CN Acharan, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L167 ANSWER 20 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 21

ACCESSION NUMBER: 1996:309677 CAPLUS

DOCUMENT NUMBER: 125:30324

TITLE: A new glycosaminoglycan from the giant African snail Achatina fulica

AUTHOR(S): Kim, Yeong S.; Jo, You Y.; Chang, Il M.; Toida, Toshihiko; Park, Youmie; Linhardt, Robert J.

CORPORATE SOURCE: Nat. Products Res. Inst., Seoul Natl. Univ., Seoul, 110-460, S. Korea

SOURCE: Journal of Biological Chemistry (1996), 271(20), 11750-11755

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A new glycosaminoglycan has been isolated from the giant African snail Achatina fulica. This polysaccharide had a mol. weight of 29,000, calculated based on the viscometry, and a uniform repeating disaccharide structure of  $\rightarrow 4$ )-2-acetyl,2-deoxy- $\alpha$ -D-glucopyranose (1 $\rightarrow$ 4)-2-sulfo- $\alpha$ -L-idopyranosyluronic acid (1 $\rightarrow$ ). This polysaccharide represents a new, previously undescribed glycosaminoglycan. It is related to the heparin and heparan sulfate families of glycosaminoglycans but is distinctly different from all known members of these classes of

glycosaminoglycans. The structure of this polysaccharide, with adjacent N-acetylglucosamine and 2-sulfo-iduronic acid residues, also poses interesting questions about how it is made in light of our current understanding of the biosynthesis of heparin and heparan sulfate. This glycosaminoglycan represents 3-5% of the dry weight of this snail's soft body tissues, suggesting important biol. roles for the survival of this organism, and may offer new means to control this pest. Snail glycosaminoglycan tightly binds divalent cations, such as copper(II), suggesting a primary role in metal uptake in the snail. Finally, this new polysaccharide might be applied, like the *Escherichia coli* K5 capsular polysaccharide, to the study of glycosaminoglycan biosynthesis and to the semisynthesis of new glycosaminoglycan analogs having important biol. activities.

CC 12-1 (Nonmammalian Biochemistry)

Section cross-reference(s): 33

IT 177791-14-9D, repeating unit

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)

(glycosaminoglycan isolation and structural characterization from giant African snail)

IT 177791-14-9D, repeating unit

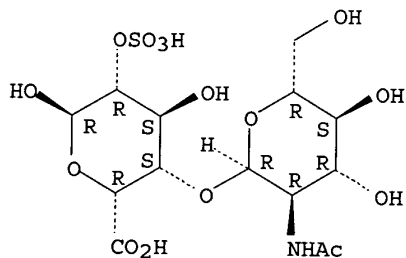
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)

(glycosaminoglycan isolation and structural characterization from giant African snail)

RN 177791-14-9 CAPLUS

CN  $\alpha$ -L-Idopyranuronic acid, 4-O-[2-(acetylamino)-2-deoxy- $\alpha$ -D-glucopyranosyl]-, 2-(hydrogen sulfate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L167 ANSWER 21 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 22  
 ACCESSION NUMBER: 1995:469480 CAPLUS  
 DOCUMENT NUMBER: 123:83881  
 TITLE: Analysis of fluorescently labeled sugars by reversed-phase ion-pairing high-performance liquid chromatography  
 AUTHOR(S): Kim, Y. S.; Liu, J.; Han, X. J.; Pervin, A.; Linhardt, R. J.  
 CORPORATE SOURCE: Natural Products Inst., Seoul Natl. Univ., Seoul, S. Korea  
 SOURCE: Journal of Chromatographic Science (1995), 33(4), 162-7  
 CODEN: JCHSBZ; ISSN: 0021-9665  
 PUBLISHER: Preston Publications  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Reducing sugars, including monosaccharides, disaccharides, and a trisaccharide, are derivatized by reductive amination with 7-amino-1,3-naphthalene disulfonic acid. Reversed-phase ion-pairing high-performance liquid chromatog. is then used to sep. these visibly fluorescent, charged conjugates. Isocratic elution with triethylamine-acetic acid from a Ph column, a C18 column, and C18 and Ph columns in series gives good sepns. of a mixture of monosaccharides and a mixture of disaccharides and trisaccharides. Resolution of certain monosaccharides and trisaccharides. Resolution of certain monosaccharides is enhanced by replacing triethylamine with a chiral amine and using gradient elution. Further enhancement of resolution is achieved by adding phenylboronic acid, an agent capable of complexing with the vicinal diol functionality present in many sugars. The trimethylamine-acetic acid eluant permits detection by either UV absorbance or fluorescence, and the addition of a chiral ion-pairing agent or a phenylboronic acid complexing agent necessitates fluorescence detection. A reversible Schiff base form of the fluorescent sugar conjugate is prepared; it is sufficient stable to perform fractionations but sufficiently unstable to be converted to a fluorescent label and reducing sugar.

CC 33-7 (Carbohydrates)

L167 ANSWER 22 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 23

ACCESSION NUMBER: 1992:443868 CAPLUS

DOCUMENT NUMBER: 117:43868

TITLE: Lectin affinity electrophoresis for the separation of fluorescently labeled sugar derivatives

AUTHOR(S): Lee, K. B.; Kim, Y. S.; Linhardt, R. J.

CORPORATE SOURCE: Coll. Pharm., Univ. Iowa, Iowa City, IA, 52242, USA

SOURCE: Analytical Biochemistry (1992), 203(2), 206-10

CODEN: ANBCA2; ISSN: 0003-2697

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Lectin affinity electrophoresis was applied to the separation of charged, fluorescent conjugates of disaccharides. Four fluorescent conjugates were prepared by reductive amination of  $\alpha$ -D-Man-(1 $\rightarrow$ 3)-D-Man,  $\alpha$ -D-Gal-(1 $\rightarrow$ 4)-D-Gal,  $\alpha$ -D-Gal-(1 $\rightarrow$ 6)-D-Glc, and  $\beta$ -D-Gal-(1 $\rightarrow$ 4)-D-Glc in the presence of 7-amino-1,3-naphthalenedisulfonic acid. These charged fluorescent-disaccharide conjugates have identical mol. weight and in the absence of Co A lectin failed to sep. either by agarose or by polyacrylamide gel electrophoresis. In the presence of either free or immobilized Con A, agarose gel electrophoresis and polyacrylamide gel electrophoresis could sep. the fluorescent conjugates of the above sugars.

CC 9-7 (Biochemical Methods)

Section cross-reference(s): 33

L167 ANSWER 23 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 24

ACCESSION NUMBER: 1992:2692 CAPLUS

DOCUMENT NUMBER: 116:2692

TITLE: Capillary zone electrophoresis for the quantitation of oligosaccharides formed through the action of chitinase

AUTHOR(S): Lee, Kyung Bok; Kim, Yeong Shik; Linhardt, Robert J.

CORPORATE SOURCE: Coll. Pharm., Univ. Iowa, Iowa City, IA, 52242, USA

SOURCE: Electrophoresis (1991), 12(9), 636-40

CODEN: ELCTDN; ISSN: 0173-0835

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Capillary zone electrophoresis with fluorescence detection was used to analyze the products formed by chitinase acting on N-acetylchitooligosaccharide-fluorescent conjugates. Six oligosaccharides of the structure [N-acetylglucosamine(1→4)]<sub>n</sub> (where n = 1-6) were conjugated to 7-amino-1,3-naphthalene disulfonic acid by reductive amination. Each oligosaccharide-fluorescent conjugate was purified by preparative gradient PAGE, semi-dry electrotransfer to a pos.-charged nylon membrane, and recovered by washing the membrane with salt solution. The products formed by treating each oligosaccharide-fluorescent conjugate with chitinase were analyzed by capillary zone electrophoresis. The chitinase treatment hexasaccharide-fluorescent conjugate was also examined kinetically to study the action pattern of this enzyme.

CC 7-3 (Enzymes)  
Section cross-reference(s): 9

L167 ANSWER 24 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 25

ACCESSION NUMBER: 1992:443130 CAPLUS  
DOCUMENT NUMBER: 117:43130  
TITLE: Detection of chitinase activity using  
fluorescence-labeled substrate on polyacrylamide gel  
AUTHOR(S): Kim, Yeong Shik; Lee, Kyung Bok;  
Linhardt, Robert J.  
CORPORATE SOURCE: Natl. Prod. Res. Inst., Seoul Natl. Univ., Seoul,  
110-460, S. Korea  
SOURCE: Han'guk Saenghwa Hakhoechi (1991), 24(5), 466-71  
CODEN: KBCJAK; ISSN: 0368-4881  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Gradient PAGE was used to analyze the products formed by chitinases acting on N-acetylchitohexaose-fluorescent conjugates. N-Acetylchitooligosaccharides were conjugated to 7-amino-1,3-naphthalenedisulfonic acid by reductive amination. Each oligosaccharide fluorescent conjugate was purified by preparative gradient PAGE, semi-dry electrotransfer to a pos.-charged nylon membrane, and recovered by washing the membrane with a salt solution. The N-acetylchitohexaose-fluorescent conjugate and chitohexaose were exhaustively treated with 3 kinds of chitinases from *Serratia marcescens*, *Streptomyces griseus*, and green onion (*Allium fistulosum*). The bands were visualized under long-UV light. Anal. of reaction products provided information on the action of chitinases from different sources.

CC 7-1 (Enzymes)

L167 ANSWER 25 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 27

ACCESSION NUMBER: 1989:88012 CAPLUS  
DOCUMENT NUMBER: 110:88012  
TITLE: Structural features of heparin and their effect on  
heparin cofactor II mediated inhibition of thrombin  
AUTHOR(S): Kim, Y. S.; Linhardt, R. J.  
CORPORATE SOURCE: Coll. Pharm., Univ. Iowa, Iowa City, IA, 52242, USA  
SOURCE: Thrombosis Research (1989), 53(1), 55-71  
CODEN: THBRAA; ISSN: 0049-3848  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Heparins from different species and tissues show similar levels of antithrombin (ATIII) and heparin cofactor II(HCII)-mediated anti-IIa activities. After fractionation, chains containing predominantly ATIII or HCII activities could not be separated. Oligosaccharide mapping demonstrated that the concentration of an oligosaccharide comprising a portion of heparin's ATIII binding site in a particular heparin fraction correlates with the ATIII-mediated anti-IIa activity, but does not correlate with the

HCII-mediated anti-IIa activity. ATIII and HCII may not share a common binding site. Partial enzymic depolarization of heparin resulted in large oligosaccharides which could be purified and partially characterized. Although oligosaccharides of d.p. 18 and 20 showed significant ATIII- and HCII-mediated anti-IIa activities, no separation of these activities resulted. Min. chain length of dpl8 was required for HCII-mediated anti-IIa activity.

CC 1-3 (Pharmacology)

L167 ANSWER 26 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 28

ACCESSION NUMBER: 1988:542049 CAPLUS

DOCUMENT NUMBER: 109:142049

TITLE: Homogeneous, structurally defined heparin-oligosaccharides with low anticoagulant activity inhibit the generation of the amplification pathway C3 convertase in vitro

AUTHOR(S): Linhardt, Robert J.; Rice, Kevin G.; Kim, Yeong S.; Engelken, John D.; Weiler, John M.

CORPORATE SOURCE: Coll. Pharm., Univ. Iowa, Iowa City, IA, 52242, USA

SOURCE: Journal of Biological Chemistry (1988), 263(26), 13090-6

CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Heparin-oligosaccharides were prepared by partial depolymn. of heparin by using purified flavobacterial heparinase. The resulting oligosaccharide mixture was then fractionated by using strong anion exchange-HPLC to produce individual oligosaccharide components of this mixture, with degree of polymerization ranging 2-16. These heparin-oligosaccharides were examined for

both their anticoagulant activity and capacity to inhibit activation of the amplification pathway of complement. Although there was little difference among com. heparins, a correlation between mol. weight and activity to inhibit convertase generation was clearly established for heparin-oligosaccharides between d.p. 2 through 16. Heparin-oligosaccharides of degree of polymerization 10-16 (Mr 3888-5320) demonstrated

up to 54% of heparin's activity on a molar basis (and up to 163% of heparin's activity on a weight basis) in inhibiting the amplification pathway of complement in vitro while showing almost no anticoagulant activity. Thus heparin-oligosaccharides with low anticoagulant activity have a high capacity to inhibit activation of the amplification pathway of complement in vitro. These studies, for the 1st time, completely sep. heparin's ability to inhibit complement activation from its anticoagulant activity.

CC 1-3 (Pharmacology)

Section cross-reference(s): 13, 15

L167 ANSWER 27 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 29

ACCESSION NUMBER: 1988:586768 CAPLUS

DOCUMENT NUMBER: 109:186768

TITLE: Mapping and quantification of the major oligosaccharide components of heparin

AUTHOR(S): Linhardt, Robert J.; Rice, Kevin G.; Kim, Yeong S.; Lohse, Daniel L.; Wang, Hui M.; Loganathan, Duraikkannu

CORPORATE SOURCE: Coll. Pharm., Univ. Iowa, Iowa City, IA, 52242, USA

SOURCE: Biochemical Journal (1988), 254(3), 781-7

CODEN: BIJOAK; ISSN: 0306-3275

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A new method of determining the oligosaccharide composition of com. glycosaminoglycan

heparin is described in which heparin was first depolymerized with heparin lyase (E.C. 4.2.2.7) and then analyzed by a single HPLC step. All 20 of the porcine and bovine heparins examined contained a small number of major oligosaccharide components, which on average comprised 86% of their mass. The 5 most abundant oligosaccharides have defined chemical structures. Although the relative abundance of oligosaccharides varied, the heparins examined were surprisingly similar. Porcine, bovine, low-Mr, and high and low antithrombin III (ATIII)-affinity heparins, however, each had distinctly different proportions of these major oligosaccharide components. The concentration of 1 of these 5 oligosaccharides, containing a portion of the

ATIII

binding site, correlated with the anticoagulant activity of the ATIII-affinity-fractionated porcine-mucosal heparins from which it was derived. An additional oligosaccharide of undetermined structure was found in significant quantities in both bovine heparin and high ATIII-affinity porcine-mucosal heparin. The correlation between oligosaccharide concentration and anticoagulant activity suggests that the oligosaccharide is derived from a structural variant of the ATIII-binding site. Finally, for the heparins examined chondroitin/dermatan sulfate formed 0.6-7.4% of their mass.

CC 9-15 (Biochemical Methods)

Section cross-reference(s): 1, 44

L167 ANSWER 28 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 30

ACCESSION NUMBER: 1988:488599 CAPLUS

DOCUMENT NUMBER: 109:88599

TITLE: Microheterogeneity of plasma glycoproteins heparin cofactor II and antithrombin III and their carbohydrate analysis

AUTHOR(S): Kim, Yeong Shik; Lee, Kyung Bok; Linhardt, Robert J.

CORPORATE SOURCE: Coll. Pharm., Univ. Iowa, Iowa City, IA, 52242, USA  
SOURCE: Thrombosis Research (1988), 51(1), 97-104  
CODEN: THBRAA; ISSN: 0049-3848

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Microheterogeneity was demonstrated for heparin cofactor II and antithrombin III. Their carbohydrate components were determined

CC 7-2 (Enzymes)

L167 ANSWER 29 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 31

ACCESSION NUMBER: 1987:439 CAPLUS

DOCUMENT NUMBER: 106:439

TITLE: Structure and activity of a unique heparin-derived hexasaccharide

AUTHOR(S): Linhardt, Robert J.; Rice, Kevin G.; Merchant, Zohar M.; Kim, Yeong S.; Lohse, Daniel L.

CORPORATE SOURCE: Coll. Pharm., Univ. Iowa, Iowa City, IA, 52242, USA  
SOURCE: Journal of Biological Chemistry (1986), 261(31), 14448-54

CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A hexasaccharide representing a major sequence in porcine mucosal heparin has been enzymically prepared from heparin. Its structure was determined by an integrated approach using chemical, enzymic, and spectroscopic methods.

Two-dimensional <sup>1</sup>H homonuclear COSY, C-H correlation NMR, and selective irradiation were used to assign many of the NMR resonances. In addition, new techniques including sulfate determination by ion chromatog. and Fourier transform

IR and californium plasma desorption mass spectroscopy have been applied, resulting in an unambiguous structural assignment of  $\Delta\text{IdoAp}2\text{S}(1\rightarrow4)-\alpha\text{-D-GlcNp}2\text{S}6\text{S}(1\rightarrow4)-\alpha\text{-L-IdoAp}(1\rightarrow4)-\alpha\text{-D-GlcNAcp}6\text{S}(1\rightarrow4)-\beta\text{-D-GlcAp}(1\rightarrow4)-\alpha\text{-D-GlcNp}2\text{S}3\text{S}6\text{S}$  [105575-57-3] (where  $\Delta\text{IdoA}$  represents 4-deoxy- $\alpha\text{-L-threo-hex-4-enopyranosyluronic acid}$ , p represents pyranose, and GlcA and IdoA represent glucuronic and iduronic acid). This hexasaccharide contains a portion of the antithrombin [9000-94-6] III-binding site and has a  $K_d$  of  $4 \times 10^{-5}\text{M}$ . Unlike other small heparin oligosaccharides, which are specific for coagulation factor Xa [9002-05-5], it inhibits both factors IIa [9002-04-4] and Xa equally through antithrombin III. This hexasaccharide may have the unique capacity to act primarily through heparin cofactor II [81604-65-1] to inhibit thrombin cofactor IIa and shows over half of heparin's heparin cofactor II-mediated anti-factor IIa activity. These studies suggest the occurrence of contiguous binding sites on heparin for Xa, antithrombin III, and heparin cofactor II.

CC 1-8 (Pharmacology)

L167 ANSWER 30 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 32

ACCESSION NUMBER: 1986:16733 CAPLUS  
DOCUMENT NUMBER: 104:16733  
TITLE: Evidence of random structural features in the heparin polymer  
AUTHOR(S): Linhardt, Robert J.; Merchant, Zohar M.; Rice, K. G.; Kim, Y. S.; Fitzgerald, Gerald L.; Grant, Arthur C.; Langer, Robert  
CORPORATE SOURCE: Coll. Pharm., Univ. Iowa, Iowa City, IA, 52242, USA  
SOURCE: Biochemistry (1985), 24(26), 7805-10  
CODEN: BICHAW; ISSN: 0006-2960  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The 1st use of computer-simulation studies to examine the structure of heparin is reported. The product distributions obtained when porcine mucosal heparins were depolymerized with heparinase were compared to computer-simulated distributions. The modeled distribution was relatively unaffected by the polydispersity and mol. weight of heparin. However, the percent of heparinase-cleavable glycosidic linkages and their distribution throughout the polymer resulted in a marked change in the simulated product distribution. The similarity between exptl. observed and computer-simulated product distributions is consistent with the random distribution of heparinase-cleavable sites in porcine mucosal heparin. Finally, a random distribution of N-acetyl residues with respect to heparinase-cleavable sites was exptl. observed

CC 6-4 (General Biochemistry)  
Section cross-reference(s): 33

L167 ANSWER 31 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 33

ACCESSION NUMBER: 1985:578553 CAPLUS  
DOCUMENT NUMBER: 103:178553  
TITLE: Structure of heparin-derived tetrasaccharides  
AUTHOR(S): Merchant, Z. M.; Kim, Y. S.; Rice, K. G.; Linhardt, R. J.  
CORPORATE SOURCE: Coll. Pharm., Univ. Iowa, Iowa City, IA, 52242, USA  
SOURCE: Biochemical Journal (1985), 229(2), 369-77  
CODEN: BIJOAK; ISSN: 0306-3275

DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The structure of heparin was examined by characterizing a disaccharide and five of the more than a dozen tetrasaccharide components obtained by its depolymn. with flavobacterial heparinase. Enzymic depolymn. of porcine mucosal heparin results in a mixture of di-, tetra-, hexa- and higher oligosaccharides. The di- and tetrasaccharide components represent 75mol/100mol of these heparin fragments. Ion-exchange chromatog. indicates the presence of only one disaccharide,  $\Delta$ Idu2S(1 $\rightarrow$ 4)- $\alpha$ -D-GlcNS6S (where Idu is iduronic acid,  $\Delta$ Idu is 4-deoxy- $\alpha$ -L-threo-hex-4-enopyranosyluronic acid, GlcN is glucosamine, GlcA is glucuronic acid and S is sulfate), but results in the solution of five major and at least seven minor tetrasaccharide components. The structures of the disaccharide and five major tetrasaccharides were determined by chemical, enzymic, electrophoretic, and spectroscopic methods, including  $^{13}\text{C}$ ,  $^1\text{H}$  NMR and fast atom bombardment mass spectrometry. The structure of these five tetrasaccharides are:  $\Delta$ Idu2S(1 $\rightarrow$ 4)- $\alpha$ -D-GlcNS6S(1 $\rightarrow$ 4)- $\alpha$ -L-Idu2S(1 $\rightarrow$ 4)- $\alpha$ -D-GlcNS6S;  $\Delta$ Idu2S(1 $\rightarrow$ 4)- $\alpha$ -D-GlcNS6S(1 $\rightarrow$ 4)- $\beta$ -D-GlcA(1 $\rightarrow$ 4)- $\alpha$ -D-GlcNS6S;  $\Delta$ Idu2S(1 $\rightarrow$ 4)- $\alpha$ -D-GlcNS(1 $\rightarrow$ 4)- $\beta$ -D-GlcA(1 $\rightarrow$ 4)- $\alpha$ -D-GlcNS6S;  $\Delta$ Idu2S(1 $\rightarrow$ 4)- $\alpha$ -D-GlcNAc(1 $\rightarrow$ 4)- $\beta$ -D-GlcA(1 $\rightarrow$ 4)- $\alpha$ -D-GlcNS6S; and  $\Delta$ Idu2S(1 $\rightarrow$ 4)- $\alpha$ -D-GlcNAc(1 $\rightarrow$ 4)- $\alpha$ -L-Idu(1 $\rightarrow$ 4)- $\alpha$ -D-GlcNS6S. The disaccharide and the five major tetrasaccharides do not possess significant anticoagulant activity.

CC 33-8 (Carbohydrates)

L167 ANSWER 32 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 34  
ACCESSION NUMBER: 1985:592544 CAPLUS  
DOCUMENT NUMBER: 103:192544  
TITLE: High-performance liquid chromatographic separation of heparin-derived oligosaccharides  
AUTHOR(S): Rice, K. G.; Kim, Y. S.; Grant, A. C.; Merchant, Z. M.; Linhardt, R. J.  
CORPORATE SOURCE: Coll. Pharm., Univ. Iowa, Iowa City, IA, 52242, USA  
SOURCE: Analytical Biochemistry (1985), 150(2), 325-31  
CODEN: ANBCA2; ISSN: 0003-2697  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Heparin was enzymically depolymd. with heparinase (heparin lyase (EC 4.2.2.7)) and then sep. into di-, tetra-, hexa-, octa-, and decasaccharide mixts. by low-pressure gel-permeation chromatog. (GPC). These sized mixts. were resolved by strong anion-exchange (SAX) HPLC into multiple components. The fractions from the SAX-HPLC were collected and characterized for size by GPC-HPLC and sulfate content by ion chromatog. This study provides detailed method for the separation of larger and more highly sulfated oligosaccharides than previously reported. It describes the 1st use of ion chromatog. for the accurate determination of the sulfate content of heparin oligosaccharides, a method which can also be applied to heparin and other glycosaminoglycans.

CC 9-3 (Biochemical Methods)

L167 ANSWER 33 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 35  
ACCESSION NUMBER: 1985:404756 CAPLUS  
DOCUMENT NUMBER: 103:4756  
TITLE: Small heparin fragments regulate the amplification pathway of complement  
AUTHOR(S): Sharath, Murali D.; Merchant, Zohar M.; Kim, Yeong S.; Rice, Kevin G.; Linhardt, Robert



J.; Weiler, John M.  
CORPORATE SOURCE: Dep. Intern. Med., Veterans Adm. Med. Cent., Iowa  
City, IA, 52242, USA  
SOURCE: Immunopharmacology (1985), 9(2), 73-80  
CODEN: IMMUDP; ISSN: 0162-3109  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Heparin is a highly sulfated, polydisperse and heterogeneous  
glycosaminoglycan which has been well characterized for its ability to  
regulate multiple sites in the complement cascade. Although previous  
studies demonstrated the relation between degree of sulfation,  
particularly O-sulfation, and complement-inhibiting capacity, they left  
unclear the relation between the size of the heparin mol. and its ability  
to inhibit complement. Therefore, although the structure-activity  
relation for heparin is well understood for anticoagulant activity, it is  
ill defined for the complement system. The present studies were designed  
to examine depolymerized heparin to determine which fragments were capable of  
inhibiting amplification pathway activation. As the size of the mol.  
increased, the ability to regulate complement increased; below 1000  
daltons the fragments were essentially inactive and above 3500 they had  
the same activity as com. heparin. Furthermore, the 5 major  
tetrasaccharides of heparin were analyzed, and the degree of sulfation did  
correlate with the ability to inhibit complement. These studies have for  
the 1st time begun to examine the minimal structural requirements for  
heparin to regulate complement.  
CC 15-4 (Immunochemistry)

L167 ANSWER 34 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1069968 CAPLUS  
DOCUMENT NUMBER: 142:458725  
TITLE: Nucleolin: **acharan sulfate**-binding  
protein on the surface of cancer cells  
AUTHOR(S): Joo, Eun Ji; Ten Dam, Gerdy B.; Van Kuppevelt, Toin  
H.; Toida, Toshihiko; Linhardt, Robert J.;  
**Kim, Yeong Shik**  
CORPORATE SOURCE: Natural Products Research Institute, College of  
Pharmacy, Seoul National University, Seoul, 110-460,  
S. Korea  
SOURCE: Glycobiology (2004), Volume Date 2005, 15(1), 1-9  
CODEN: GLYCE3; ISSN: 0959-6658  
PUBLISHER: Oxford University Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Glycosaminoglycans (GAGs) are complex polysaccharides that participate in  
the regulation of physiol. processes through the interactions with a wide  
variety of proteins. **Acharan sulfate** (AS), isolated from the  
giant African snail *Achatina fulica*, primarily consists of the repeating  
disaccharide structure  $\alpha$ -D-N-acetylglucosaminyl (1 $\rightarrow$ 4)  
2-sulfoiduronic acid. Exogenous AS was injected s.c. near the tumor  
tissue in C57BL/6 mice that had been implanted with Lewis lung carcinoma  
cells (LLCs). The location of AS in the tumor was assessed by staining of  
sectioned tissues with alcian blue and periodic acid-Schiff (PAS) reagent.  
In vitro assays indicated binding of cells to 50  $\mu$ g/mL AS (or heparin)  
after a 5-h incubation. Immunofluorescence assays, using anti-AS  
antibody, detected AS at the cell surface. The outer-surface of LLCs were  
next biotinylated to identify the AS-binding proteins. Biotinylated cells  
were lysed, and the lysates were fractionated on the AS affinity column  
using a stepwise salt gradient (0, 0.1, 0.3, 0.5, 0.7, 1.0, and 2.0 M).  
The fractions were analyzed by SDS-PAGE with silver staining and western  
blotting. We focused on the proteins with high affinity for AS (eluting

at 1 M NaCl) and detected only two bands by western blotting. ESI Q-TOF MS anal. of one of these bands, mol. weight .apprx.110 kDa, showed it to be nucleolin. A phosphorylated form of nucleolin on the surface of cells acts as a cell surface receptor for a variety of ligands, including growth factors (i.e., basic fibroblast growth factor) and chemokines (i.e., midkine). These results show that nucleolin is one of several AS-binding proteins and suggest that AS might demonstrate its tumor growth inhibitory activity by binding the nucleolin receptor protein on the surface of cancer cells.

CC 6-3 (General Biochemistry)  
 ST nucleolin **acharan sulfate** protein membrane cancer  
 IT Lung, neoplasm  
     (carcinoma; purification and characterization of nucleolin, a **acharan sulfate**-binding protein of cell membrane of cancer cells)

IT Proteins  
 RL: BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)  
     (nucleolins; purification and characterization of nucleolin, a **acharan sulfate**-binding protein of cell membrane of cancer cells)

IT Carcinoma  
     (pulmonary; purification and characterization of nucleolin, a **acharan sulfate**-binding protein of cell membrane of cancer cells)

IT Cell membrane  
 Neoplasm  
     (purification and characterization of nucleolin, a **acharan sulfate**-binding protein of cell membrane of cancer cells)

IT 192662-57-0, **Acharan sulfate**  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
     (purification and characterization of nucleolin, a **acharan sulfate**-binding protein of cell membrane of cancer cells)

IT 192662-57-0, **Acharan sulfate**  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
     (purification and characterization of nucleolin, a **acharan sulfate**-binding protein of cell membrane of cancer cells)

RN 192662-57-0 CAPLUS  
 CN Acharan, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L167 ANSWER 35 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:34040 CAPLUS

DOCUMENT NUMBER: 128:97878

TITLE: Glycosaminoglycans can influence fibroblast growth factor-2 mitogenicity without significant growth factor binding. [Erratum to document cited in CA127:117569]

AUTHOR(S): Wang, Huiming; Toida, Toshihiko; Kim, Yeong Shik; Capila, Ishan; Hileman, Ronald E.; Bernfield, Merton; Linhardt, Robert J.

CORPORATE SOURCE: Department of Pediatrics, Harvard Medical School, Boston, MA, 02115, USA

SOURCE: Biochemical and Biophysical Research Communications (1998), 242(1), 248

PUBLISHER: CODEN: BBRCA9; ISSN: 0006-291X Academic Press

DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB On page 372, the legend to Fig. 3 misidentified the square, circle, and open and closed triangles used in the figure; Fig. 3 and its correct legend are given.  
CC 2-5 (Mammalian Hormones)  
IT 9005-49-6, Heparin, biological studies 106096-93-9, Basic fibroblast growth factor **192662-56-9**, N-Sulfoacharan sulfate **192662-57-0**, **Acharan sulfate**  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(glycosaminoglycans influence FGF-2 mitogenicity without growth factor binding (Erratum))  
IT **192662-56-9**, N-Sulfoacharan sulfate **192662-57-0**, **Acharan sulfate**  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(glycosaminoglycans influence FGF-2 mitogenicity without growth factor binding (Erratum))  
RN 192662-56-9 CAPLUS  
CN Acharan, N-deacetyl-N-sulfo, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 192662-57-0 CAPLUS  
CN Acharan, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L167 ANSWER 36 OF 47 MEDLINE on STN DUPLICATE 3  
ACCESSION NUMBER: 2005009866 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 15329357  
TITLE: Nucleolin: **acharan sulfate**-binding protein on the surface of cancer cells.  
AUTHOR: Joo Eun Ji; ten Dam Gerdy B; van Kuppevelt Toin H; Toida Toshihiko; **Linhardt Robert J; Kim Yeong Shik**  
CORPORATE SOURCE: Natural Products Research Institute, College of Pharmacy, Seoul National University, 28 Yeonkun-Dong, Jongno-Ku, Seoul 110-460, Korea.  
SOURCE: Glycobiology, (2005 Jan) 15 (1) 1-9. Electronic Publication: 2004-08-25.  
Journal code: 9104124. ISSN: 0959-6658.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200505  
ENTRY DATE: Entered STN: 20050108  
Last Updated on STN: 20050517  
Entered Medline: 20050516

ABSTRACT:

Glycosaminoglycans (GAGs) are complex polysaccharides that participate in the regulation of physiological processes through the interactions with a wide variety of proteins. **Acharan sulfate** (AS), isolated from

the giant African snail *Achatina fulica*, primarily consists of the repeating disaccharide structure alpha-D-N-acetylglucosaminyl (1-->4) 2-sulfoiduronic acid. Exogenous AS was injected subcutaneously near the tumor tissue in C57BL/6 mice that had been implanted with Lewis lung carcinoma cells (LLCs). The location of AS in the tumor was assessed by staining of sectioned tissues with alcian blue and periodic acid-Schiff (PAS) reagent. In vitro assays indicated binding of cells to 50 microg/ml AS (or heparin) after a 5-h incubation. Immunofluorescence assays, using anti-AS antibody, detected AS at the cell surface. The outer-surface of LLCs were next biotinylated to identify the AS-binding proteins. Biotinylated cells were lysed, and the lysates were fractionated on the AS affinity column using a stepwise salt gradient (0, 0.1, 0.3, 0.5, 0.7, 1.0, and 2.0 M). The fractions were analyzed by SDS-PAGE with silver staining and western blotting. We focused on the proteins with high affinity for AS (eluting at 1 M NaCl) and detected only two bands by western blotting. ESI Q-TOF MS analysis of one of these bands, molecular weight approximately 110 kDa, showed it to be nucleolin. A phosphorylated form of nucleolin on the surface of cells acts as a cell surface receptor for a variety of ligands, including growth factors (i.e., basic fibroblast growth factor) and chemokines (i.e., midkine). These results show that nucleolin is one of several AS-binding proteins and suggest that AS might demonstrate its tumor growth inhibitory activity by binding the nucleolin receptor protein on the surface of cancer cells.

CONTROLLED TERM: Amino Acid Sequence  
 Animals  
 Blotting, Western  
 Cell Adhesion  
 Cell Line, Tumor  
 \*Cell Membrane: ME, metabolism  
 Electrophoresis, Polyacrylamide Gel  
 \*Glycosaminoglycans: ME, metabolism  
 Humans  
 Mice  
 Mice, Inbred C57BL  
 Molecular Sequence Data  
 \*Neoplasms: ME, metabolism  
 \*Neoplasms: PA, pathology  
 Phosphoproteins: CH, chemistry  
 Phosphoproteins: IP, isolation & purification  
 \*Phosphoproteins: ME, metabolism  
 RNA-Binding Proteins: CH, chemistry  
 RNA-Binding Proteins: IP, isolation & purification  
 \*RNA-Binding Proteins: ME, metabolism  
 Research Support, Non-U.S. Gov't  
 Spectrum Analysis, Mass  
 CHEMICAL NAME: 0 (Glycosaminoglycans); 0 (Phosphoproteins); 0 (RNA-Binding Proteins); 0 (**acharan sulfate**); 0 (nucleolin)

L167 ANSWER 37 OF 47 MEDLINE on STN DUPLICATE 26  
 ACCESSION NUMBER: 91297473 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 2068567  
 TITLE: Molecular profile and mapping of dermatan sulfates from different origins.  
 AUTHOR: Linhardt R J; al-Hakim A; Liu S Y; Kim Y S; Fareed J  
 CORPORATE SOURCE: Division of Medicinal and Natural Products Chemistry, College of Pharmacy, University of Iowa, Iowa City 52242.  
 CONTRACT NUMBER: GM38060 (NIGMS)  
 HL29797 (NHLBI)  
 SOURCE: Seminars in thrombosis and hemostasis, (1991) 17 Suppl 1

15-22.

Journal code: 0431155. ISSN: 0094-6176.

PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199108  
ENTRY DATE: Entered STN: 19910901  
Last Updated on STN: 19910901  
Entered Medline: 19910809

## ABSTRACT:

A method for characterization and molecular profiling of acidic polysaccharides (such as dermatan sulfates) has been developed. A variety of dermatan sulfates, fractionated dermatan sulfates and low molecular weight dermatan sulfates, were examined. First, bacterial lyase-type enzymes (chondroitinase ABC) were used to depolymerize the polysaccharides. Then, mapping of these oligosaccharides (comparable to peptide mapping of proteins) was performed using gradient PAGE and SAX-HPLC. Bands and peaks observed in these maps were identified using oligosaccharide standards of defined chemical structures and physical properties. The resulting map can be used to point to structural differences among these dermatan sulfates regarding their size, charge, degree of sulfation, and contamination. Fine details of fragmentation patterns and absence or presence of contaminants were detected by silver staining of gels. These differences, particularly the content of----4)alpha-IdoA(1----3)-beta-D-GalNAc4S6S(1----sequences (detected using SAX-HPLC as delta UA(1----3)-beta-D-GalNAc4S6S) may play an important role influencing the activity of dermatan sulfates to potentiate HC II inhibition of Factor IIa.

CONTROLLED TERM: Check Tags: Comparative Study  
Animals  
Carbohydrate Sequence  
Cattle  
Chromatography, Gel  
Chromatography, High Pressure Liquid  
\*Dermatan Sulfate: CH, chemistry  
Dermatan Sulfate: IP, isolation & purification  
Electrophoresis, Polyacrylamide Gel  
Intestines: CH, chemistry  
Molecular Sequence Data  
Mucous Membrane: CH, chemistry  
Research Support, Non-U.S. Gov't  
Research Support, U.S. Gov't, P.H.S.  
Skin: CH, chemistry  
Swine

CAS REGISTRY NO.: 24967-94-0 (Dermatan Sulfate)

L167 ANSWER 38 OF 47 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1999:258319 BIOSIS

DOCUMENT NUMBER: PREV199900258319

TITLE: Heparin, chemically modified heparins, and Acharan  
**sulfate** differentially regulate complement activity.

AUTHOR(S): Edens, R. Erik [Reprint author]; Kim, Yeong S.;  
Wu, Song J.; Linhardt, Robert J.; Caldwell,  
Elizabeth B.; Weiler, John M.

CORPORATE SOURCE: Pediatrics, University of Iowa, Iowa City, IA, USA  
SOURCE: Pediatric Research, (April, 1999) Vol. 45, No. 4 PART 2,  
pp. 22A. print.  
Meeting Info.: Annual Meeting of the American Pediatric  
Society and the Society for Pediatric Research. San

Francisco, California, USA. May 1-4, 1999.  
CODEN: PEREBL. ISSN: 0031-3998.

DOCUMENT TYPE: Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
Conference; (Meeting Poster)

LANGUAGE: English

ENTRY DATE: Entered STN: 2 Jul 1999  
Last Updated on STN: 2 Jul 1999

CONCEPT CODE: Pharmacology - Immunological processes and allergy 22018  
Metabolism - Carbohydrates 13004  
Metabolism - Proteins, peptides and amino acids 13012  
Immunology - Immunopathology, tissue immunology 34508  
Pharmacology - Drug metabolism and metabolic stimulators 22003  
General biology - Symposia, transactions and proceedings 00520  
Biochemistry studies - Proteins, peptides and amino acids 10064  
Biochemistry studies - Carbohydrates 10068  
Biophysics - Molecular properties and macromolecules 10506

INDEX TERMS: Major Concepts  
Immune System (Chemical Coordination and Homeostasis);  
Pharmacology

INDEX TERMS: Chemicals & Biochemicals  
**acharan sulfate**: immunologic-drug,  
complement activity regulator; chemically modified  
heparin: immunologic-drug, complement activity  
regulator; heparin: immunologic-drug, complement  
activity regulator

INDEX TERMS: Miscellaneous Descriptors  
Meeting Abstract; Meeting Poster

ORGANISM: Classifier  
Animalia 33000  
Super Taxa  
Animalia  
Organism Name  
animal: animal model  
Taxa Notes  
Animals

REGISTRY NUMBER: 192662-57-0 (**acharan sulfate**)  
9005-49-6 (heparin)

L167 ANSWER 39 OF 47 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN

ACCESSION NUMBER: 1997:420074 BIOSIS

DOCUMENT NUMBER: PREV199799719277

TITLE: **Acharan sulfate** and **acharan sulfate**-derived new oligosaccharides.

AUTHOR(S): **Kim, Yeong Shik** [Reprint author]; Ahn, Mi Young  
[Reprint author]; Shin, Kuk Hyun [Reprint author]; Woo,  
Song Ji [Reprint author]; Chun, Moon Woo; Kim, Dong-Hyun;  
Toida, Toshihiko; **Linhardt, Robert J.**

CORPORATE SOURCE: Natural Prod. Res. Inst., Seoul Natl. Univ., Seoul, South  
Korea

SOURCE: FASEB Journal, (1997) Vol. 11, No. 9, pp. A995.  
Meeting Info.: 17th International Congress of Biochemistry  
and Molecular Biology in conjunction with the Annual  
Meeting of the American Society for Biochemistry and  
Molecular Biology. San Francisco, California, USA. August

24-29, 1997.  
CODEN: FAJOEC. ISSN: 0892-6638.

DOCUMENT TYPE: Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 8 Oct 1997  
Last Updated on STN: 21 Nov 1997

CONCEPT CODE: General biology - Symposia, transactions and proceedings  
00520  
Biochemistry studies - Carbohydrates 10068  
Biophysics - Methods and techniques 10504

INDEX TERMS: Major Concepts  
Biochemistry and Molecular Biophysics; Methods and  
Techniques

INDEX TERMS: Chemicals & Biochemicals  
**ACHARAN SULFATE**

INDEX TERMS: Miscellaneous Descriptors  
**ACHARAN SULFATE**;  
ALPHA-D-N-ACETYLGLUCOSAMINYL 2-SULFO-IDURONIC ACID;  
ANALYTICAL METHOD; BIOCHEMISTRY AND BIOPHYSICS; GIANT  
AFRICAN SNAIL; GLYCOSAMINOGLYCAN; HIGH PERFORMANCE  
LIQUID CHROMATOGRAPHY; NMR SPECTROSCOPY

ORGANISM: Classifier  
Gastropoda 61200  
Super Taxa  
Mollusca; Invertebrata; Animalia  
Organism Name  
Achatina fulica  
Taxa Notes  
Animals, Invertebrates, Mollusks

REGISTRY NUMBER: 192662-57-0 (**ACHARAN SULFATE**)

L167 ANSWER 40 OF 47 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN

ACCESSION NUMBER: 1988:368228 BIOSIS

DOCUMENT NUMBER: PREV198835052841; BR35:52841

TITLE: FUNDAMENTAL OLIGOSACCHARIDES DERIVED FROM HEPARIN AND THEIR  
CORRELATION TO ANTICOAGULANT ACTIVITY.

AUTHOR(S): **LINHARDT R J** [Reprint author]; **RICE K G**; **KIM  
Y S**; **LOHSE D L**; **WANG H M**; **LOGANATHAN D**

CORPORATE SOURCE: DIV MED AND NATURAL PRODUCTS CHEM, COLL PHARMACY, UNIV  
IOWA, IOWA CITY, IOWA 52242, USA

SOURCE: Abstracts of Papers Chemical Congress of North America,  
(1988) Vol. 3, No. 1, pp. CARB 100.  
Meeting Info.: THIRD CHEMICAL CONGRESS OF NORTH AMERICA  
HELD AT THE 195TH AMERICAN CHEMICAL SOCIETY MEETING,  
TORONTO, ONTARIO, CANADA, JUNE 5-10, 1988. ABSTR PAP CHEM  
CONGR NORTH AM.

DOCUMENT TYPE: Conference; (Meeting)

FILE SEGMENT: BR

LANGUAGE: ENGLISH

ENTRY DATE: Entered STN: 9 Aug 1988  
Last Updated on STN: 9 Aug 1988

CONCEPT CODE: General biology - Symposia, transactions and proceedings  
00520  
Biochemistry studies - Carbohydrates 10068  
Pharmacology - Blood and hematopoietic agents 22008

INDEX TERMS: Major Concepts  
Biochemistry and Molecular Biophysics; Pharmacology

INDEX TERMS: Miscellaneous Descriptors

ABSTRACT  
REGISTRY NUMBER: 9005-49-6 (HEPARIN)

L167 ANSWER 41 OF 47 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN

ACCESSION NUMBER: 1987:246464 BIOSIS  
DOCUMENT NUMBER: PREV198732121722; BR32:121722  
TITLE: GRADIENT PAGE AND STRONG ANION EXCHANGE SAX HPLC AS  
ANALYTICAL TOOLS FOR SEQUENCING THE HEPARIN POLYMER.  
AUTHOR(S): RICE K G [Reprint author]; KIM Y S; LOHSE D L;  
LINHARDT R J  
CORPORATE SOURCE: DIV MEDICINAL NAT PROD CHEM, COLL PHARMACY, UNIV IOWA, IOWA  
CITY, IA 52242, USA  
SOURCE: Abstracts of Papers American Chemical Society, (1987) Vol.  
193.  
Meeting Info.: 193RD AMERICAN CHEMICAL SOCIETY NATIONAL  
MEETING, DENVER, COLORADO, USA, APRIL 5-10, 1987. ABSTR PAP  
AM CHEM SOC.  
CODEN: ACSRAL. ISSN: 0065-7727.  
DOCUMENT TYPE: Conference; (Meeting)  
FILE SEGMENT: BR  
LANGUAGE: ENGLISH  
ENTRY DATE: Entered STN: 26 May 1987  
Last Updated on STN: 26 May 1987  
CONCEPT CODE: General biology - Symposia, transactions and proceedings  
00520  
Biochemistry methods - Carbohydrates 10058  
Biochemistry studies - Carbohydrates 10068  
Biophysics - Methods and techniques 10504  
Biophysics - Molecular properties and macromolecules  
10506  
INDEX TERMS: Major Concepts  
Biochemistry and Molecular Biophysics  
INDEX TERMS: Miscellaneous Descriptors  
ABSTRACT POLYACRYLAMIDE GEL ELECTROPHORESIS HIGH  
PERFORMANCE LIQUID CHROMATOGRAPHY  
REGISTRY NUMBER: 9005-49-6D (HEPARIN)  
9003-05-8 (POLYACRYLAMIDE)

L167 ANSWER 42 OF 47 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN

ACCESSION NUMBER: 1985:133146 BIOSIS  
DOCUMENT NUMBER: PREV198529023142; BR29:23142  
TITLE: SMALL HEPARIN FRAGMENTS INHIBIT COMPLEMENT ACTIVATION.  
AUTHOR(S): LINHARDT R J [Reprint author]; SHARATH M D;  
MERCHANT Z M; KIM Y S; RICE K G; WEILER J M  
CORPORATE SOURCE: DIV MEDICINAL CHEMISTRY, COLLEGE OF PHARMACY, UNIVERSITY OF  
IOWA, IOWA CITY, IOWA 52242, USA  
SOURCE: Federation Proceedings, (1985) Vol. 44, No. 4, pp. 989.  
Meeting Info.: 69TH ANNUAL MEETING OF THE FEDERATION OF  
AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, ANAHEIM,  
CALIF., USA, APR. 21-26, 1985. FED PROC.  
CODEN: FEPA7. ISSN: 0014-9446.  
DOCUMENT TYPE: Conference; (Meeting)  
FILE SEGMENT: BR  
LANGUAGE: ENGLISH  
CONCEPT CODE: General biology - Symposia, transactions and proceedings  
00520  
Biochemistry studies - Proteins, peptides and amino acids  
10064



Biochemistry studies - Carbohydrates 10068  
Biophysics - Molecular properties and macromolecules 10506  
Enzymes - Physiological studies 10808  
Metabolism - Proteins, peptides and amino acids 13012  
Blood - Blood and lymph studies 15002  
Immunology - General and methods 34502  
Immunology - Immunopathology, tissue immunology 34508

INDEX TERMS: Major Concepts  
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Enzymology (Biochemistry and Molecular Biophysics); Immune System (Chemical Coordination and Homeostasis); Metabolism

INDEX TERMS: Miscellaneous Descriptors  
ABSTRACT ALTERNATIVE PATHWAY CONVERTASE GENERATION

REGISTRY NUMBER: 9005-49-6 (HEPARIN)

L167 ANSWER 43 OF 47 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1986:46797 BIOSIS  
DOCUMENT NUMBER: PREV198630046797; BR30:46797  
TITLE: VERY LOW MOLECULAR WEIGHT HEPARIN FRAGMENT INHIBITION OF COMPLEMENT ACTIVATION.

AUTHOR(S): LINHARDT R J [Reprint author]; KIM Y S; MERCHANT Z M; RICE G H; WEILER J M

CORPORATE SOURCE: DEP MED CHEM NATURAL PRODUCTS, COLLEGE PHARMACY, UNIV IOWA, IOWA CITY, IOWA, USA

SOURCE: Complement, (1985) Vol. 2, No. 1, pp. 49.  
Meeting Info.: 11TH INTERNATIONAL COMPLEMENT WORKSHOP, MIAMI, FLA., USA, NOV. 3-5, 1985. COMPLEMENT.  
CODEN: CMLPDF. ISSN: 0253-5076.

DOCUMENT TYPE: Conference; (Meeting)  
FILE SEGMENT: BR  
LANGUAGE: ENGLISH  
ENTRY DATE: Entered STN: 25 Apr 1986  
Last Updated on STN: 25 Apr 1986

CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520  
Biochemistry studies - Proteins, peptides and amino acids 10064  
Biochemistry studies - Carbohydrates 10068  
Biophysics - Molecular properties and macromolecules 10506  
Blood - Blood and lymph studies 15002  
Immunology - Immunopathology, tissue immunology 34508

INDEX TERMS: Major Concepts  
Blood and Lymphatics (Transport and Circulation); Immune System (Chemical Coordination and Homeostasis)

INDEX TERMS: Miscellaneous Descriptors  
ABSTRACT

REGISTRY NUMBER: 9005-49-6 (HEPARIN)

L167 ANSWER 44 OF 47 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1986:79732 BIOSIS  
DOCUMENT NUMBER: PREV198630079732; BR30:79732  
TITLE: BIOLOGICAL ACTIVITY OF VERY LOW MOLECULAR WEIGHT HEPARIN OLIGOSACCHARIDES.

AUTHOR(S): MERCHANT Z M [Reprint author]; KIM Y S; RICE K G; LOHSE D L; LINHARDT R J

CORPORATE SOURCE: DIV MEDICINAL CHEM NAT PRODUCTS, COLL PHARMACY, UNIV IOWA,  
IOWA CITY, IA 52242, USA

SOURCE: Abstracts of Papers American Chemical Society, (1985) Vol.  
190.  
Meeting Info.: 190TH AMERICAN CHEMICAL SOCIETY NATIONAL  
MEETING, CHICAGO, ILL., USA, SEPT. 8-13, 1985. ABSTR PAP AM  
CHEM SOC.  
CODEN: ACSRAL. ISSN: 0065-7727.

DOCUMENT TYPE: Conference; (Meeting)

FILE SEGMENT: BR

LANGUAGE: ENGLISH

ENTRY DATE: Entered STN: 25 Apr 1986  
Last Updated on STN: 25 Apr 1986

CONCEPT CODE: General biology - Symposia, transactions and proceedings  
00520  
Biochemistry studies - Proteins, peptides and amino acids  
10064  
Biochemistry studies - Carbohydrates 10068  
Biophysics - Molecular properties and macromolecules  
10506  
Cardiovascular system - Blood vessel pathology 14508  
Blood - Blood and lymph studies 15002  
Endocrine - General 17002  
Pharmacology - Blood and hematopoietic agents 22008  
Pharmacology - Cardiovascular system 22010

INDEX TERMS: Major Concepts  
Blood and Lymphatics (Transport and Circulation);  
Cardiovascular System (Transport and Circulation);  
Endocrine System (Chemical Coordination and  
Homeostasis); Pharmacology

INDEX TERMS: Miscellaneous Descriptors  
ABSTRACT ANTICOAGULANT-DRUG ANTIATHEROSCLEROTIC  
COMPLEMENT INHIBITION

REGISTRY NUMBER: 9005-49-6 (HEPARIN)

L167 ANSWER 45 OF 47 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN

ACCESSION NUMBER: 1986:79762 BIOSIS

DOCUMENT NUMBER: PREV198630079762; BR30:79762

TITLE: ISOLATION AND CHARACTERIZATION OF LOW MOLECULAR WEIGHT  
HEPARIN DERIVED OLIGOSACCHARIDES.

AUTHOR(S): MERCHANT Z M [Reprint author]; KIM Y S; RICE K G;  
LOHSE D L; LINHARDT R J

CORPORATE SOURCE: DIV MED CHEM NAT PRODUCTS, COLL PHARMACY, UNIV IOWA, IOWA  
CITY, IA 52242, USA

SOURCE: Abstracts of Papers American Chemical Society, (1985) Vol.  
190.  
Meeting Info.: 190TH AMERICAN CHEMICAL SOCIETY NATIONAL  
MEETING, CHICAGO, ILL., USA, SEPT. 8-13, 1985. ABSTR PAP AM  
CHEM SOC.  
CODEN: ACSRAL. ISSN: 0065-7727.

DOCUMENT TYPE: Conference; (Meeting)

FILE SEGMENT: BR

LANGUAGE: ENGLISH

ENTRY DATE: Entered STN: 25 Apr 1986  
Last Updated on STN: 25 Apr 1986

CONCEPT CODE: General biology - Symposia, transactions and proceedings  
00520  
Biochemistry methods - Carbohydrates 10058  
Biochemistry studies - Carbohydrates 10068

Biophysics - Molecular properties and macromolecules  
10506  
Cardiovascular system - Blood vessel pathology 14508  
Blood - Blood, lymphatic and reticuloendothelial  
pathologies 15006  
Pharmacology - Blood and hematopoietic agents 22008  
Pharmacology - Cardiovascular system 22010

INDEX TERMS: Major Concepts  
Biochemistry and Molecular Biophysics; Blood and  
Lymphatics (Transport and Circulation); Cardiovascular  
System (Transport and Circulation); Pharmacology

INDEX TERMS: Miscellaneous Descriptors  
ABSTRACT ANTICOAGULANT-DRUG ANTITHROMBOTIC STRUCTURE  
ACTIVITY RELATIONSHIP

REGISTRY NUMBER: 9005-49-6 (HEPARIN)

L167 ANSWER 46 OF 47 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN

ACCESSION NUMBER: 1985:87569 BIOSIS  
DOCUMENT NUMBER: PREV198528087569; BR28:87569  
TITLE: ENZYMATIC PREPARATION OF ANTICOAGULANTS FROM HEPARIN.  
AUTHOR(S): LINHARDT R J [Reprint author]; MERCHANT Z M;  
KIM Y S; RICE K G  
CORPORATE SOURCE: DIV MED CHEM, UNIV IOWA COLL PHARMACY, IOWA CITY, IOWA  
52242, USA  
SOURCE: Abstracts of Papers American Chemical Society, (1984) Vol.  
188.  
Meeting Info.: 188TH AMERICAN CHEMICAL SOCIETY MEETING,  
PHILADELPHIA, PA., USA, AUG. 26-31, 1984. ABSTR PAP AM CHEM  
SOC.  
CODEN: ACSRAL. ISSN: 0065-7727.  
Conference; (Meeting)

DOCUMENT TYPE: BR  
FILE SEGMENT: ENGLISH  
LANGUAGE: ENGLISH  
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TITLE: Antitumor inhibitors and use thereof

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Kim, Yeong Shik, Seoul, KOREA, REPUBLIC OF

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CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides pharmaceutical compositions for the treatment of **cancer** and inhibiting an increase in the volume or mass of a **tumor**, and methods for the treatment of **cancer** and inhibiting an increase in the volume or mass of a **tumor**.

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TI Antitumor inhibitors and use thereof

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AB The present invention provides pharmaceutical compositions for the treatment of **cancer** and inhibiting an increase in the volume or mass of a **tumor**, and methods for the treatment of **cancer** and inhibiting an increase in the volume or mass of a **tumor**.

SUMM [0003] **Angiogenesis**, or neovascularization, is the formation of new capillaries from preexisting blood vessels and is a fundamental process involved in a . . . of physiological (Folkman, 1971; Folkman, 1972; Folkman and Shing, 1992) and pathophysiological processes (Folkman, 1995; Carmeliet and Jain, 2000). In **cancer**, this process contributes to the progressive growth and metastasis of solid **tumors**. (Liotta et al., 1991).

SUMM [0004] **Tumor angiogenesis** is regulated by the production of **angiogenic** stimulators including members of fibroblast growth factor (FGF) and vascular endothelial growth factor (VEGF) families (Colville-Nash and Willoughby, 1997; Kim et al., 1993). Drugs that interfere with **angiogenesis**, by halting the action of **angiogenic** proteins, might reduce the size of **tumors** and maintain them in a dormant state. **Angiogenic** inhibitors such as angiostatin and endostatin can modulate **angiogenesis** both at the primary site and at the downstream sites of metastasis (O'Reilly et al, 1994, 1997). The potential use of

these and other natural and synthetic **angiogenesis** inhibitors is currently being studied intensively by many laboratories (Mohan et al., 2000; Suh et al., 1997; Minamiguchi et al., . . .

SUMM [0005] Heparin/heparan sulfate interacts with various **angiogenic** growth factors (Capila and Linhardt, 2002). **Angiogenic** growth factors induce response in target endothelial cells by binding to cognate cell-surface tyrosine kinase receptors (Gale and Yancopoulos, 1999). The interaction of heparin-binding growth factors to tyrosine kinase receptors is modulated by heparan sulfate proteoglycans. **Acharan sulfate** (AS) isolated from the giant African snail, *Achatina fulica*, is a novel member of glycosaminoglycan (GAG) family (Kim et al., . . . HPLC-GPC analysis. Recently, we observed that AS interfered with heparin's bFGF mitogenicity in vitro, suggesting its possible utility as an **angiogenesis** inhibitor (Wang et al., 1997).

SUMM [0006] U.S. Pat. No. 6,028,061 describes and claims the use of AS in inhibiting **angiogenesis** based on its inhibition of FGF (fibroblast growth hormone). We have now discovered that AS has **antitumor** activity as demonstrated in both in vivo and in vitro assays. The in vivo **antitumor** activity is demonstrated against the **sarcoma** 180-induced solid **tumor** and primary **tumor** in LLC-bearing C57BL/6 mice. This is the first demonstration of in vivo **antitumor** activity using AS ever observed. Although more than 30 years ago it was hypothesized that **tumor** growth is **angiogenesis** dependent (Folkman, 1971) anti-**angiogenesis** activity does not predict in vivo **tumor** growth inhibition. Thus, the present invention provides a marked advance in the elucidation of useful in vivo anti-**tumor** agents.

SUMM [0007] The present invention provides pharmaceutical compositions for the treatment of **cancer** and for inhibiting an increase in the volume or mass of a **tumor** in a host in need of treatment. The present invention also provides methods for the treatment of **cancer** and for the inhibition of an increase in the volume or mass of a **tumor** in a host in need of treatment. Compounds which are the active ingredients of the compositions and methods of the.

SUMM [0009] The present invention is based on the discovery that **acharan sulfate** demonstrates in vivo anti-**tumor** activity. Thus, a novel method of inhibiting **tumor** growth and treating **cancer** is provided by the present invention. As used herein **acharan sulfate** means a glycosaminoglycan from the giant African snail, *Achatina fulica* having primarily the repeating disaccharide structure of  $\alpha$ -D-N-acetylglucosaminyl 2-sulfoalduronic acid. . . .

DRWD [0010] FIG. 1 depicts the structure of **acharan sulfate** . And the site of its structure where it can be cleaved using heparin lyase II.

DRWD [0011] FIG. 2 is a photograph of a control egg and one treated with **acharan sulfate** showing the effect of **acharan sulfate** on inhibition of **angiogenesis**.

DRWD [0012] FIG. 3 shows the effect of **acharan sulfate** on bFGF-induced **angiogenesis** in mouse model.

DRWD [0013] FIG. 4 shows the effect of **acharan sulfate** on calf pulmonary endothelial cell proliferation by MTT assay.

DRWD [0014] FIG. 5 shows the effect of **acharan sulfate** on **tumor** volume in Lewis lung **carcinoma**-bearing mice.

DRWD [0015] FIG. 6 shows the effect of **acharan sulfate** on **tumor** weight in Lewis lung **carcinoma**-bearing mice.

DRWD [0016] FIG. 7 shows effects of **acharan sulfate** on

tumor volume (A) and tumor weight (B) in  
sarcoma 180-bearing mice.

DRWD [0017] FIG. 8 shows effect of **acharan sulfate** on  
survival time of mice **sarcoma** with 180 ascitic tumor

DETD [0018] **Acharan sulfate** is a glucosaminoglycan having  
a repeating disaccharide structure described as  $\rightarrow 4$ )- $\alpha$ -D-  
GlcNpAc(1 $\rightarrow$ 4)- $\alpha$ -L-IdoAp2S(1 $\rightarrow$ , where GlcNpAc is  
2-acetamido 2-deoxyglucopyranose, IdoAp is idopyranosyluronic acid.

DETD . . . embodiment of the present invention is the use of and  
compositions comprising compounds of Formula I for the treatment of  
**cancer** or for inhibiting an increase in the mass or volume of a  
**tumor** in a patient in need of treatment wherein n is 4 to 100  
and more preferably 4 to 50. The pharmaceutical compositions of the  
present invention are useful in the treatment of **cancer** and in  
the inhibition of an increase in the volume or mass of a **tumor**  
in a patient in need of treatment. The use of the compounds of Formula I  
is directed to a method of treating **cancer** and of inhibiting  
an increase in the mass or volume of a **tumor** in a patient in  
need of treatment.

DETD [0022] Described herein are experiments carried out to evaluate the  
**antiangiogenic** activity of **acharan sulfate**.  
We also show herein that **acharan sulfate** inhibits  
new blood vessel formation in the in vivo matrigel and chorioallantoic  
membrane assays. Additionally, we show that **acharan**  
**sulfate** has substantial **antitumor** activity against  
**sarcoma** 180-induced solid and primary **tumors** in Lewis  
lung **carcinoma**-bearing C57BL/6 mice.

DETD Preparation of **Acharan Sulfate**

DETD [0023] **Acharan sulfate** was isolated from the soft  
body tissue of the giant African snail by proteolysis of defatted tissue  
and purified by. . .

DETD Characterization of **Acharan Sulfate**

DETD [0025] The invention provides compositions and methods that can be used  
to treat **cancer** utilizing the compounds of Formula I. These  
compounds are shown herein to inhibit a gain in mass or volume of a  
**tumor**. Accordingly, these compounds may be administered to an  
animal in need of such treatment, including warm blooded animals, such  
as. . . art. Furthermore, these compounds may be formulated as  
pharmaceutical dosage forms containing an effective amount of the  
compound to inhibit **tumors** from gaining mass or volume. In  
addition, the compounds of the invention can be formulated as single  
unit dosage forms.. . .

DETD . . . effective dosage of a compound of Formulae I for inhibition of  
an increase in the volume or mass of a **tumor** or as an  
**anticancer** agent is extrapolated from the results of the in vivo  
studies set forth herein. The effective dosage is dependent not. . .

DETD [0038] Lewis lung **carcinoma** cells (American Type Cell  
Collection, Rockville, Md.) were maintained in DMEM supplemented with  
heat-inactivated 10% FBS (Life Technologies, Grand Island, N.Y.), 100  
units/ml penicillin, and 100  $\mu$ g/ml streptomycin. Calf pulmonary  
arterial endothelial (CPAE) cells and **sarcoma** 180 (Korea Cell  
Line Bank, Seoul, Korea) were cultured in RPMI 1640 media containing 10%  
FBS and 1% antibiotics in. . .

DETD [0039] The effect of **acharan sulfate** on the  
inhibition of **angiogenesis** was performed using the  
chorioallantoic membrane (CAM) assay. These assays essentially followed  
previously published procedures (Tanaka et al, 1986; Oikawa. . . half  
days later, sample-loaded thermanox coverslips (Nunc, Naperville, Ill.)

were air-dried and applied to the CAM surface for testing of **angiogenesis** inhibition by AS. Two days later, 1 ml of 10% fat emulsion (Intralipose) was injected into the chorioallantoic membrane and the avascular zone was observed under a dissecting microscope. Inhibition of **angiogenesis** was assessed when the avascular zone exceeded 3 mm. In order to abolish the possibility of contaminant in AS, the depolymerized product by heparinase II as described above was also tested for the **antiantiogenic** activity. The concentration of AS used in this assay was selected based on the concentration of heparin that had previously.

DETD . . . AS on the treated CAM is shown in FIG. 2 and Table 1.

TABLE 1

Effect of AS on chick embryonic **angiogenesis**

| Compounds                   | Concen-<br>tration<br>(µg/egg) | Eggs showing<br>antiangio-<br>genesis.sup.a | Total eggs<br>tested | % inhibition |
|-----------------------------|--------------------------------|---|----------------------|--------------|
| Control (H.sub.20) --       |                                | 3   | 54                   | 5.6          |
| Retinoic acid.sup.b 1       |                                | 20  | 25                   | 80.0         |
| Acharan sulfate 50          |                                | 2   | 40                   |              |
| 5.0                         |                                |   |                      |              |
| depolymerization<br>mixture |                                |   |                      |              |
| Acharan sulfate I 5         |                                | 14  | 29                   |              |
| 48.3                        |                                |   |                      |              |
| Acharan sulfate II 10       |                                | 15  | 27                   |              |
| 55.6                        |                                |   |                      |              |

.sup.a**Antiantiogenesis** was assessed when the avascular zone exceeded 3 mm.

.sup.bRetinoic acid was used as a positive control.

DETD [0042] Compared to the effect of vehicle as control, which did not have **antiantiogenic** activity in the treated CAM, AS at doses of 5 and 10 µg/pellet showed **antiantiogenic** activity of 48.3 and 55.6%, respectively. The effect of AS on chick embryonic **angiogenesis** decreased in a dose-dependent fashion. Retinoic acid strongly inhibited **angiogenesis** (80%) even at 1 µg/egg, but it may have a toxic effect to cells. The depolymerization mixture of AS by heparin lyase II did not cause any inhibition of **angiogenesis**, indicating that any contaminant in the intact AS could not act as an **angiogenic** inhibitor.

DETD [0043] The effect of **acharan sulfate** on the inhibition of **angiogenesis** was also evaluated in the matrigel plug assay. This assay was performed as previously described (Passaniti et al., 1992). **Acharan sulfate**, dissolved in water, bFGF and heparin, dissolved in 0.1% bovine serum albumen (BSA)/phosphate buffered saline (PBS) were mixed with liquid.

DETD [0044] To evaluate the effect of AS on ongoing **angiogenic** process in the mouse matrigel plug assay matrigel, heparin (10 units/500 µl), and bFGF (100 ng/500 µl) with or without. . . blood cells, indicating the formation of a functional vasculature inside the matrigel and blood circulation in newly formed vessels by **angiogenesis** induced by bFGF and heparin. Fifty micrograms of AS in combination with bFGF and heparin slightly prevented the vessel induction, indicating that AS suppressed the bFGF-stimulated **angiogenesis**. We next measured the hemoglobin content inside the matrigel plugs to quantify the **angiogenesis**. Whereas bFGF and heparin increased Hb concentration to 11.8 g/dl and the Hb concentration inside the control

- was 0.3 g/dl, . . . (FIG. 3). Each value represents mean $\pm$ S.E.M. of at least 5 animals. The data are significantly different from the control; \*\*P<0.01 Anti-**angiogenesis** in this assay did not result from the effect of a vehicle of bFGF and the injection sites showed no signs of inflammation and hemorrhage. Anti-**angiogenesis** in this assay did not result from the effect of a vehicle of bFGF and the injection sites showed no. . .
- DETD [0045] The effect of **acharan sulfate** on in vitro cell proliferation was carried out using calf pulmonary artery endothelial (CPAE) cells as follows.
- DETD [0048] The effect of AS in vivo on **tumor** growth was evaluated as follows.
- DETD [0049] Male C57BL/6 mice were inoculated s.c. in the back with LLC cells (1+10.sup.6/animal) on day 0. After **tumor** volume was at least 60-100 mm.sup.3, AS was administered into the subcutaneous region near the **tumor** mass at two doses of 10 and 30 mg/kg for 15 days. The size of **tumors** in all groups was measured using a dial-caliper and the volume of **tumors** was determined using the formula width.sup.2+length+0.52 (Voest et al., 1995; Cao et al., 1995). The effects of AS on **tumor** growth and host survival were also measured by evaluating **tumor** volumes, **tumor** weights and percentage increase in lifespan of **tumor** hosts, respectively (Oguchi et al., 1987; Kusumoto, 1991). For calculating the survival time, mice were inoculated i.p. with 106 **sarcoma** 180 cells/mouse on day 0 and the treatment with two doses of AS (50 and 100 mg/kg, i.p.) were started. . . days. The control group was treated with saline. Median survival time (MST) for each group (n=7) was observed and the **antitumor** activity of the test compounds were compared with that of control group by measuring the increase in lifespan.
- DETD [0050] For solid **tumor** development, ICR mice were injected with 0.1 ml of **sarcoma** 180 suspensions into the right hind limbs. After 6 days of **tumor** transplantation, mice randomized into six groups were injected i.p. with AS (50 and 100 mg/kg) and 5-FU (25 mg/kg) once a day for 9 days. Eight days later after treatment, animals were sacrificed by cervical dissociation, and solid **tumors** were removed and weighed.
- DETD [0051] The results of AS on **tumor** growth in C57BL/6 mice inoculated with Lewis lung **carcinoma** cells are shown in FIGS. 5 and 6. A daily subcutaneous injection of 10 and 30 mg/kg suppressed the growth of primary **tumors** during the 15-day treatment course. At the end of treatment, **tumor** growth was inhibited by 32.8% (3049.2 mm.sup.3) and 38.1% (2809.3 mm.sup.3), respectively at a dose of 10 mg/kg and 30 mg/kg, as compared to control mice treated with saline alone (4534.4 mm.sup.3). In contrast, **tumor** grew rapidly to sizes >4000 mm.sup.3 in saline-treated mice during the same 15-day treatment period. Doxorubicin as positive control was administered i.v. every five day at a dose of 10 mg/kg. It inhibited **tumor** growth by 62.0% (1721.6 mm.sup.3). The AS-treated mice did not lose weight over the course of treatment, indicating that AS showed little or no toxicity. On day 21, **tumor** tissues were removed and weighed. It was found that the **tumor** weight was reduced dose-dependently by the injection of AS as shown in FIG. 6. A mean **tumor** weight reductions by 37.8% (2.8 $\pm$ 0.2 g) at 10 mg/kg and by 48.9% (2.3 $\pm$ 0.2 g) at 30 mg/kg were observed, compared with the saline group (4.5 $\pm$ 0.7 g). Doxorubicin significantly reduced the **tumor** weight by 68.0% (1.6 $\pm$ 0.2 g). However, the loss of weight in the group of the doxorubicin-treated mice was marked as. . .
- DETD [0052] The results of the effect of AS on solid **tumor** induced by **sarcoma** 180 **tumor** cells in ICR are shown in FIG.



7. As shown in FIG. 7A, the average **tumor** volume in the control was  $8804 \pm 465.3$  mm<sup>3</sup>. The level of the **tumor** volume in groups treated with 5-FU injection decreased by 82.1% ( $1572 \pm 201.5$  mm<sup>3</sup>), compared with the control level. AS at the dose of 50 mg/kg inhibited the **tumor** volume by 45.0% ( $4799 \pm 345.2$  mm<sup>3</sup>). AS at the dose of 50 mg/kg inhibited the **tumor** weight by 39.6% ( $4.3 \pm 0.1$  g), while 5-FU at the dose of 25 mg/kg inhibited the **tumor** weight by 75.1% ( $1.8 \pm 0.3$  g) and 55.8% ( $3.1 \pm 0.3$  g), compared with the control ( $7.1 \pm 0.1$  g) (FIG. 7B). The data were. . .

- DETD [0053] The results of the effect of AS on the survival time in **sarcoma** 180 bearing mice are summarized in FIG. 8. The median survival time in the control was  $22.4 \pm 2.2$  days, while it. . .
- DETD [0055] The foregoing results show that **acharan sulfate** acts as **angiogenesis** inhibitor and in an **antitumor** agent in vivo. Based on the above results AS does not influence proliferation of endothelial cells as demonstrated in the. . . results show that AS markedly inhibits the development of capillary networks at two concentrations (5 and 10  $\mu$ g/CAM). Further the **antiangiogenic** activity of AS was confirmed by performing in vivo mouse matrigel plug assay. AS inhibited the formation of neovessels induced by a combination of bFGF and heparin in matrigel. In the foregoing experiments to evaluate the **antitumor** effect of AS in mice bearing murine LLC **tumors**, AS was given by daily subcutaneous injections at a site distant from the primary **tumor**. We speculated that one of the mechanisms for the **antiangiogenic** action of AS might be the suppression of matrix metalloprotease activity. However, AS shows no detectable antiprotease activity. AS also shows substantial **antitumor** activity against **sarcoma** 180-induced solid **tumor** and primary **tumor** in LLC-bearing C57BL/6 mice. A remarkable increase in lifespan was observed in **sarcoma** 180 ascitic **tumor**. Ascites fluids are direct nutritional sources for **tumor** cells.
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CLM

What is claimed is:

1. A method of treating **cancer** in a host in need of treatment comprising administering to said host an anti-**cancer** effective amount of a compound of the formula  $[\rightarrow 4)-\alpha\text{-D-GlcNpAc}(1\rightarrow 4)-\alpha\text{-L-IdoAp}2\text{S}(1\rightarrow)n$  wherein GlcNpAc is 2-acetamido 2-deoxyglucopyranose, IdoAp is idopyranosyluronic acid and S. . . .

6. A method of treating a host by inhibiting an increase in the volume or mass of a **tumor** in said host in need of treatment which comprises administering to said host a compound of the formula  $[\rightarrow 4)-\alpha\text{-D-GlcNpAc}(1\rightarrow 4)-\alpha\text{-L-IdoAp}2\text{S}(1\rightarrow)n$  wherein. . . n is 1 to 1000 in an amount effective to inhibit an increase in the volume or mass of a **tumor**.

. . . IdoAp is idopyranosyluronic acid and S is sulfate, and n is 1 to 1000 in an amount effective to treat **cancer** in a host by inhibiting **cancer** growth in said host

. . . and n is 1 to 1000 that is effective in inhibiting an increase in the volume or mass of a **tumor** in a host in need of such inhibiting effect.

IT 192662-57-0, Acharan sulfate  
(I and II; antitumor angiogenesis inhibitor acharan sulfate)

IT 192662-57-0, Acharan sulfate  
(I and II; antitumor angiogenesis inhibitor acharan sulfate)

RN 192662-57-0 USPATFULL

CN Acharan, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)

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L22         9 SEA FILE=CAPLUS ABB=ON  PLU=ON  L2 (L) (THU OR DMA OR PAC OR
          PKT OR BAC)/RL
L23         25 SEA FILE=CAPLUS ABB=ON  PLU=ON  ACHARAN SULFATE/OBI
L25         1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ACHARAN SULFATE/CN
L26         1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ACHARAN, N-DEACETYL-N-SULFO?/
          CN
L27         24 SEA FILE=CAPLUS ABB=ON  PLU=ON  L25
L28         5 SEA FILE=CAPLUS ABB=ON  PLU=ON  L26
L33         28 SEA FILE=CAPLUS ABB=ON  PLU=ON  ACHARAN?/BI
L36         28 SEA FILE=CAPLUS ABB=ON  PLU=ON  L33 OR L27 OR L28 OR L23
L37         304372 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?CANCER?/BI
L38         526763 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?TUMOR?/BI
L39         3949 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?TUMOUR?/BI
L40         49768 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?SARCOMA?/BI
L41         444230 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?NEOPLAS?/BI
L42         251331 SEA FILE=CAPLUS ABB=ON  PLU=ON  ?CARCINO?/BI
L44         7 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L37 OR L38 OR L39 OR L40 OR
          L41 OR L42) AND (L21 OR L22 OR L36)
```

=&gt; d que nos L45

L1 STR

```

L2      50 SEA FILE=REGISTRY SSS SAM L1
L3      1062 SEA FILE=REGISTRY SSS FUL L1
L18     STR
L20     79 SEA FILE=REGISTRY SUB=L3 SSS FUL L18
L21     33 SEA FILE=CAPLUS ABB=ON PLU=ON L20
L22     9 SEA FILE=CAPLUS ABB=ON PLU=ON L2 (L) (THU OR DMA OR PAC OR
        PKT OR BAC)/RL
L23     25 SEA FILE=CAPLUS ABB=ON PLU=ON ACHARAN SULFATE/OBI
L25     1 SEA FILE=REGISTRY ABB=ON PLU=ON ACHARAN SULFATE/CN
L26     1 SEA FILE=REGISTRY ABB=ON PLU=ON ACHARAN, N-DEACETYL-N-SULFO?/
        CN
L27     24 SEA FILE=CAPLUS ABB=ON PLU=ON L25
L28     5 SEA FILE=CAPLUS ABB=ON PLU=ON L26
L33     28 SEA FILE=CAPLUS ABB=ON PLU=ON ACHARAN?/BI
L36     28 SEA FILE=CAPLUS ABB=ON PLU=ON L33 OR L27 OR L28 OR L23
L43     34965 SEA FILE=CAPLUS ABB=ON PLU=ON ?ANGIOGEN?/BI
L45     4 SEA FILE=CAPLUS ABB=ON PLU=ON L43 AND (L21 OR L22 OR L36)

```

=> s (L44-L45) not L161

L168 4 ((L44 OR L45)) NOT L161

*printed with author search*

=> file medline

FILE 'MEDLINE' ENTERED AT 15:40:08 ON 22 FEB 2006

FILE LAST UPDATED: 21 FEB 2006 (20060221/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 will soon be available. For details on the 2005 reload, enter HELP RLOAD at an arrow prompt (=>). See also:

<http://www.nlm.nih.gov/mesh/>  
[http://www.nlm.nih.gov/pubs/techbull/nd04/nd04\\_mesh.html](http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html)  
[http://www.nlm.nih.gov/pubs/techbull/nd05/nd05\\_med\\_data\\_changes.html](http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html)  
[http://www.nlm.nih.gov/pubs/techbull/nd05/nd05\\_2006\\_MeSH.html](http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html)

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate

=> d que nos L51

```

L1      STR
L3      1062 SEA FILE=REGISTRY SSS FUL L1
L18     STR
L20     79 SEA FILE=REGISTRY SUB=L3 SSS FUL L18
L51     0 SEA FILE=MEDLINE ABB=ON PLU=ON L20

```

=> d que nos L52

```

L25     1 SEA FILE=REGISTRY ABB=ON PLU=ON ACHARAN SULFATE/CN
L52     0 SEA FILE=MEDLINE ABB=ON PLU=ON L25

```

=> d que nos L53

```
L26      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ACHARAN, N-DEACETYL-N-SULFO?/
          CN
L53      0 SEA FILE=MEDLINE ABB=ON  PLU=ON  L26
```

=> d que nos L55

```
L1        STR
L3        1062 SEA FILE=REGISTRY SSS FUL L1
L18       STR
L20       79 SEA FILE=REGISTRY SUB=L3 SSS FUL L18
L54       SEL  PLU=ON  L20 1- CHEM :      80 TERMS
L55       0 SEA FILE=MEDLINE ABB=ON  PLU=ON  L54
```

=> d que nos L69

```
L25      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ACHARAN SULFATE/CN
L26      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ACHARAN, N-DEACETYL-N-SULFO?/
          CN
L50      18 SEA FILE=MEDLINE ABB=ON  PLU=ON  ACHARAN?
L56      SEL  PLU=ON  L25 1- CHEM :      2 TERMS
L57      18 SEA FILE=MEDLINE ABB=ON  PLU=ON  L56
L58      SEL  PLU=ON  L26 1- CHEM :      2 TERMS
L59      4 SEA FILE=MEDLINE ABB=ON  PLU=ON  L58
L60      18 SEA FILE=MEDLINE ABB=ON  PLU=ON  L50 OR L57 OR L59
L61      579828 SEA FILE=MEDLINE ABB=ON  PLU=ON  ?CANCER?
L62      790107 SEA FILE=MEDLINE ABB=ON  PLU=ON  ?TUMOR?
L63      133927 SEA FILE=MEDLINE ABB=ON  PLU=ON  ?TUMOUR?
L64      125245 SEA FILE=MEDLINE ABB=ON  PLU=ON  ?SARCOMA?
L65      1548799 SEA FILE=MEDLINE ABB=ON  PLU=ON  ?NEOPLAS?
L66      575010 SEA FILE=MEDLINE ABB=ON  PLU=ON  ?CARCINO?
L67      1627678 SEA FILE=MEDLINE ABB=ON  PLU=ON  NEOPLASMS+NT/CT
L68      3636 SEA FILE=MEDLINE ABB=ON  PLU=ON  ANGIOGENESIS INHIBITORS/CT
L69      4 SEA FILE=MEDLINE ABB=ON  PLU=ON  L60 AND (L61 OR L62 OR L63 OR
          L64 OR L65 OR L66 OR L67 OR L68)
```

=> d que nos L72

```
L25      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ACHARAN SULFATE/CN
L26      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ACHARAN, N-DEACETYL-N-SULFO?/
          CN
L50      18 SEA FILE=MEDLINE ABB=ON  PLU=ON  ACHARAN?
L56      SEL  PLU=ON  L25 1- CHEM :      2 TERMS
L57      18 SEA FILE=MEDLINE ABB=ON  PLU=ON  L56
L58      SEL  PLU=ON  L26 1- CHEM :      2 TERMS
L59      4 SEA FILE=MEDLINE ABB=ON  PLU=ON  L58
L60      18 SEA FILE=MEDLINE ABB=ON  PLU=ON  L50 OR L57 OR L59
L71      30590 SEA FILE=MEDLINE ABB=ON  PLU=ON  ?ANGIOGEN?
L72      2 SEA FILE=MEDLINE ABB=ON  PLU=ON  L60 AND L71
```

=> s (L51-L53 or L55 or L69 or L72) not L162

```
L169      3 ((L51 OR L52 OR L53) OR L55 OR L69 OR L72) NOT L162
```

*printed with  
author search*

=> file embase

FILE 'EMBASE' ENTERED AT 15:40:14 ON 22 FEB 2006  
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FILE COVERS 1974 TO 20 Feb 2006 (20060220/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

=> d que nos L78

```
L1          STR
L3          1062 SEA FILE=REGISTRY SSS FUL L1
L18         STR
L20         79 SEA FILE=REGISTRY SUB=L3 SSS FUL L18
L78         0 SEA FILE=EMBASE ABB=ON PLU=ON L20
```

=> d que nos L79

```
L25         1 SEA FILE=REGISTRY ABB=ON PLU=ON ACHARAN SULFATE/CN
L79         0 SEA FILE=EMBASE ABB=ON PLU=ON L25
```

=> d que nos L80

```
L26         1 SEA FILE=REGISTRY ABB=ON PLU=ON ACHARAN, N-DEACETYL-N-SULFO?/
CN
L80         0 SEA FILE=EMBASE ABB=ON PLU=ON L26
```

=> d que nos L82

```
L1          STR
L3          1062 SEA FILE=REGISTRY SSS FUL L1
L18         STR
L20         79 SEA FILE=REGISTRY SUB=L3 SSS FUL L18
L81         SEL PLU=ON L20 1- CHEM :      80 TERMS
L82         0 SEA FILE=EMBASE ABB=ON PLU=ON L81
```

=> d que nos L96

```
L25         1 SEA FILE=REGISTRY ABB=ON PLU=ON ACHARAN SULFATE/CN
L26         1 SEA FILE=REGISTRY ABB=ON PLU=ON ACHARAN, N-DEACETYL-N-SULFO?/
CN
L77         16 SEA FILE=EMBASE ABB=ON PLU=ON ACHARAN?
L83         SEL PLU=ON L25 1- CHEM :      2 TERMS
L84         16 SEA FILE=EMBASE ABB=ON PLU=ON L83
L85         SEL PLU=ON L26 1- CHEM :      2 TERMS
L86         4 SEA FILE=EMBASE ABB=ON PLU=ON L85
L87         16 SEA FILE=EMBASE ABB=ON PLU=ON L77 OR L84 OR L86
L88         851781 SEA FILE=EMBASE ABB=ON PLU=ON ?CANCER?
L89         778474 SEA FILE=EMBASE ABB=ON PLU=ON ?TUMOR? OR ?TUMOUR?
L90         90530 SEA FILE=EMBASE ABB=ON PLU=ON ?SARCOMA?
L91         230147 SEA FILE=EMBASE ABB=ON PLU=ON ?NEOPLAS?
```

L92 517907 SEA FILE=EMBASE ABB=ON PLU=ON ?CARCINO?  
L93 34532 SEA FILE=EMBASE ABB=ON PLU=ON ?ANGIOGEN?  
L94 1349056 SEA FILE=EMBASE ABB=ON PLU=ON NEOPLASM+NT/CT  
L95 4217 SEA FILE=EMBASE ABB=ON PLU=ON ANGIOGENESIS INHIBITOR/CT  
L96 4 SEA FILE=EMBASE ABB=ON PLU=ON L87 AND (L88 OR L89 OR L90 OR  
L91 OR L92 OR L93 OR L94 OR L95)

=> s (L78 or L79 or L80 or L82 or L96) not L163

L170 2 (L78 OR L79 OR L80 OR L82 OR L96) NOT L163

=> file biosis

FILE 'BIOSIS' ENTERED AT 15:40:19 ON 22 FEB 2006  
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FILE COVERS 1969 TO DATE.  
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT  
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 15 February 2006 (20060215/ED)

=> d que nos L102

L1 STR  
L3 1062 SEA FILE=REGISTRY SSS FUL L1  
L18 STR  
L20 79 SEA FILE=REGISTRY SUB=L3 SSS FUL L18  
L102 0 SEA FILE=BIOSIS ABB=ON PLU=ON L20

=> d que nos L106

L1 STR  
L3 1062 SEA FILE=REGISTRY SSS FUL L1  
L18 STR  
L20 79 SEA FILE=REGISTRY SUB=L3 SSS FUL L18  
L105 SEL PLU=ON L20 1- CHEM : 80 TERMS  
L106 0 SEA FILE=BIOSIS ABB=ON PLU=ON L105

=> d que nos L118

L25 1 SEA FILE=REGISTRY ABB=ON PLU=ON ACHARAN SULFATE/CN  
L26 1 SEA FILE=REGISTRY ABB=ON PLU=ON ACHARAN, N-DEACETYL-N-SULFO?/  
CN  
L101 22 SEA FILE=BIOSIS ABB=ON PLU=ON ACHARAN?  
L103 17 SEA FILE=BIOSIS ABB=ON PLU=ON L25  
L104 1 SEA FILE=BIOSIS ABB=ON PLU=ON L26  
L107 SEL PLU=ON L25 1- CHEM : 2 TERMS  
L108 21 SEA FILE=BIOSIS ABB=ON PLU=ON L107  
L109 SEL PLU=ON L26 1- CHEM : 2 TERMS  
L110 4 SEA FILE=BIOSIS ABB=ON PLU=ON L109  
L111 22 SEA FILE=BIOSIS ABB=ON PLU=ON L101 OR L103 OR L104 OR L108  
OR L110  
L112 546518 SEA FILE=BIOSIS ABB=ON PLU=ON ?CANCER?  
L113 976062 SEA FILE=BIOSIS ABB=ON PLU=ON ?TUMOR? OR ?TUMOUR?  
L114 95426 SEA FILE=BIOSIS ABB=ON PLU=ON ?SARCOMA?



L115 759144 SEA FILE=BIOSIS ABB=ON PLU=ON ?NEOPLAS?  
 L116 507193 SEA FILE=BIOSIS ABB=ON PLU=ON ?CARCINO?  
 L117 35893 SEA FILE=BIOSIS ABB=ON PLU=ON ?ANGIOGEN?  
 L118 4 SEA FILE=BIOSIS ABB=ON PLU=ON L111 AND (L112 OR L113 OR L114  
 OR L115 OR L116 OR L117)

=> s (L102 or L106 or L118) not L164

L171 2 (L102 OR L106 OR L118) NOT L164

*printed with author search*

=> file wpix

FILE 'WPIX' ENTERED AT 15:40:23 ON 22 FEB 2006  
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FILE LAST UPDATED: 17 FEB 2006 <20060217/UP>  
 MOST RECENT DERWENT UPDATE: 200612 <200612/DW>  
 DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,  
 PLEASE VISIT:  
[http://www.stn-international.de/training\\_center/patents/stn\\_guide.pdf](http://www.stn-international.de/training_center/patents/stn_guide.pdf) <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE  
<http://scientific.thomson.com/support/patents/coverage/latestupdates/>

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER  
 GUIDES, PLEASE VISIT:  
<http://scientific.thomson.com/support/products/dwpi/>

>>> FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT  
 DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX  
 FIRST VIEW - FILE WPIFV.  
 FOR FURTHER DETAILS:  
<http://scientific.thomson.com/support/products/dwpifv/>

>>> THE CPI AND EPI MANUAL CODES WILL BE REVISED FROM UPDATE 200601.  
 PLEASE CHECK:  
<http://scientific.thomson.com/support/patents/dwpieref/reftools/classification>

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE  
[http://www.stn-international.de/stndatabases/details/ipc\\_reform.html](http://www.stn-international.de/stndatabases/details/ipc_reform.html) and  
<http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf> <<<

=> d que nos L159

L135 120107 SEA FILE=USPATFULL ABB=ON PLU=ON ?CANCER?  
 L136 104777 SEA FILE=USPATFULL ABB=ON PLU=ON ?TUMOR?  
 L137 12054 SEA FILE=USPATFULL ABB=ON PLU=ON ?TUMOUR?  
 L138 34800 SEA FILE=USPATFULL ABB=ON PLU=ON ?SARCOMA?  
 L139 37564 SEA FILE=USPATFULL ABB=ON PLU=ON ?NEOPLAS?  
 L140 67199 SEA FILE=USPATFULL ABB=ON PLU=ON ?CARCINO?  
 L141 22227 SEA FILE=USPATFULL ABB=ON PLU=ON ?ANGIOGEN?  
 L156 5 SEA FILE=WPIX ABB=ON PLU=ON ACHARAN?  
 L157 119623 SEA FILE=WPIX ABB=ON PLU=ON (L135 OR L136 OR L137 OR L138 OR  
 L139 OR L140 OR L141)  
 L159 3 SEA FILE=WPIX ABB=ON PLU=ON L156 AND L157

=> d que nos L152

L18 STR  
L151 1 SEA FILE=WPIX SSS FUL L18  
L152 1 SEA FILE=WPIX ABB=ON PLU=ON L151/DCR

=> d que nos L158

L18 STR  
L135 120107 SEA FILE=USPATFULL ABB=ON PLU=ON ?CANCER?  
L136 104777 SEA FILE=USPATFULL ABB=ON PLU=ON ?TUMOR?  
L137 12054 SEA FILE=USPATFULL ABB=ON PLU=ON ?TUMOUR?  
L138 34800 SEA FILE=USPATFULL ABB=ON PLU=ON ?SARCOMA?  
L139 37564 SEA FILE=USPATFULL ABB=ON PLU=ON ?NEOPLAS?  
L140 67199 SEA FILE=USPATFULL ABB=ON PLU=ON ?CARCINO?  
L141 22227 SEA FILE=USPATFULL ABB=ON PLU=ON ?ANGIOGEN?  
L151 1 SEA FILE=WPIX SSS FUL L18  
L152 1 SEA FILE=WPIX ABB=ON PLU=ON L151/DCR  
L157 119623 SEA FILE=WPIX ABB=ON PLU=ON (L135 OR L136 OR L137 OR L138 OR  
L139 OR L140 OR L141)  
L158 0 SEA FILE=WPIX ABB=ON PLU=ON L152 AND L157

=> s (L159 or L152 or L158) not L165

L172 2 (L159 OR L152 OR L158) NOT L165

*printed with  
author search*

=> file uspatfull

FILE 'USPATFULL' ENTERED AT 15:40:28 ON 22 FEB 2006  
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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 21 Feb 2006 (20060221/PD)  
FILE LAST UPDATED: 21 Feb 2006 (20060221/ED)  
HIGHEST GRANTED PATENT NUMBER: US7003800  
HIGHEST APPLICATION PUBLICATION NUMBER: US2006037120  
CA INDEXING IS CURRENT THROUGH 21 Feb 2006 (20060221/UPCA)  
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 21 Feb 2006 (20060221/PD)  
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2005  
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2005

=> d que nos L128

L1 STR  
L3 1062 SEA FILE=REGISTRY SSS FUL L1  
L18 STR  
L20 79 SEA FILE=REGISTRY SUB=L3 SSS FUL L18  
L127 SEL PLU=ON L20 1- CHEM : 80 TERMS  
L128 0 SEA FILE=USPATFULL ABB=ON PLU=ON L127

=> d que nos L142

L1 STR  
L3 1062 SEA FILE=REGISTRY SSS FUL L1  
L18 STR  
L20 79 SEA FILE=REGISTRY SUB=L3 SSS FUL L18  
L25 1 SEA FILE=REGISTRY ABB=ON PLU=ON ACHARAN SULFATE/CN

```

L26      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ACHARAN, N-DEACETYL-N-SULFO?/
          CN
L124     1 SEA FILE=USPATFULL ABB=ON  PLU=ON  L20
L125     2 SEA FILE=USPATFULL ABB=ON  PLU=ON  L25
L126     1 SEA FILE=USPATFULL ABB=ON  PLU=ON  L26
L129     SEL  PLU=ON  L25 1- CHEM :      2 TERMS
L130     4 SEA FILE=USPATFULL ABB=ON  PLU=ON  L129
L131     SEL  PLU=ON  L26 1- CHEM :      2 TERMS
L132     1 SEA FILE=USPATFULL ABB=ON  PLU=ON  L131
L133     4 SEA FILE=USPATFULL ABB=ON  PLU=ON  ACHARAN?
L134     5 SEA FILE=USPATFULL ABB=ON  PLU=ON  L124 OR L125 OR L126 OR
          L130 OR L132 OR L133
L135     120107 SEA FILE=USPATFULL ABB=ON  PLU=ON  ?CANCER?
L136     104777 SEA FILE=USPATFULL ABB=ON  PLU=ON  ?TUMOR?
L137     12054 SEA FILE=USPATFULL ABB=ON  PLU=ON  ?TUMOUR?
L138     34800 SEA FILE=USPATFULL ABB=ON  PLU=ON  ?SARCOMA?
L139     37564 SEA FILE=USPATFULL ABB=ON  PLU=ON  ?NEOPLAS?
L140     67199 SEA FILE=USPATFULL ABB=ON  PLU=ON  ?CARCINO?
L141     22227 SEA FILE=USPATFULL ABB=ON  PLU=ON  ?ANGIOGEN?
L142     4 SEA FILE=USPATFULL ABB=ON  PLU=ON  L134 AND (L135 OR L136 OR
          L137 OR L138 OR L139 OR L140 OR L141)

```

=> s (L128 or L142) not L166

L173

2 (L128 OR L142) NOT L166

*printed with author search*

=> => dup rem L168 L169 L170 L171 L172 L173

FILE 'CAPLUS' ENTERED AT 15:42:45 ON 22 FEB 2006

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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FILE 'MEDLINE' ENTERED AT 15:42:45 ON 22 FEB 2006

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PROCESSING COMPLETED FOR L168

PROCESSING COMPLETED FOR L169

PROCESSING COMPLETED FOR L170

PROCESSING COMPLETED FOR L171

PROCESSING COMPLETED FOR L172

PROCESSING COMPLETED FOR L173

L174 8 DUP REM L168 L169 L170 L171 L172 L173 (7 DUPLICATES REMOVED)

ANSWERS '1-4' FROM FILE CAPLUS

ANSWER '5' FROM FILE MEDLINE

ANSWER '6' FROM FILE WPIX

ANSWERS '7-8' FROM FILE USPATFULL

=> d ibib abs hitind hitstr L174 1-4; d iall L174 5; d ibib abs hitstr L174 6; d  
ibib abs kwic hitstr L174 7-8

L174 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1  
 ACCESSION NUMBER: 2004:727950 CAPLUS

DOCUMENT NUMBER: 141:376745

TITLE: Detection of 2-O-sulfated iduronate and  
 N-acetylglucosamine units in heparan sulfate by an  
 antibody selected against **acharan**  
**sulfate** (IdoA2S-GlcNAc)n

AUTHOR(S): ten Dam, Gerdy B.; van de Westerlo, Els M. A.;  
 Smetsters, Toon F. C. M.; Willemse, Marieke; van  
 Muijen, Goos N. P.; Merry, Catherine L. R.; Gallagher,  
 John T.; Kim, Yeong S.; van Kuppevelt, Toin H.

CORPORATE SOURCE: Departments of Biochemistry and Pathology, Nijmegen  
 Center for Molecular Life Sciences, University Medical  
 Center Nijmegen, Nijmegen, 6500 HB, Neth.

SOURCE: Journal of Biological Chemistry (2004), 279(37),  
 38346-38352

PUBLISHER: CODEN: JBCHA3; ISSN: 0021-9258  
 American Society for Biochemistry and Molecular  
 Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The snail glycosaminoglycan **acharan** sulfate (AS) is structurally  
 related to heparan sulfates (HS) and has a repeating disaccharide  
 structure of  $\alpha$ -D-N-acetylglucosaminyl-2-O-sulfo- $\alpha$ -L-iduronic  
 acid (GlcNAc-IdoA2S) residues. Using the phage display technol., a unique  
 antibody (MW3G3) was selected against AS with a VH3, DP 47, and a CDR3  
 amino acid sequence of QKKRPRF. Antibody MW3G3 did not react with  
 desulfated, N-deacetylated or N-sulfated AS, indicating that reactivity  
 depends on N-acetyl and 2-O-sulfate groups. Antibody MW3G3 also had a  
 high preference for (modified) heparin oligosaccharides containing  
 N-acetylated glucosamine and 2-O-sulfated iduronic acid residues. In  
 tissues, antibody MW3G3 identified a HS oligosaccharide epitope containing  
 N-acetylated glucosamine and 2-O-sulfated iduronic acid residues as  
 enzymic N-deacetylation of HS in situ prevented staining, and  
 2-O-sulfotransferase-deficient Chinese hamster ovary cells were not  
 reactive. An immunohistochem. survey using various rat organs revealed a  
 distinct distribution of the MW3G3 epitope, which was primarily present in  
 the basal laminae of most (but not all) blood vessels and of some  
 epithelia, including human skin. No staining was observed in the  
 glycosaminoglycan-rich **tumor** matrix of metastatic melanoma. In  
 conclusion, we have selected an antibody that identifies HS  
 oligosaccharides containing N-acetylated glucosamine and 2-O-sulfated iduronic  
 acid residues. This antibody may be instrumental in identifying  
 structural alterations in HS in health and disease.

CC 9-16 (Biochemical Methods)

IT Blood vessel

Human

Melanoma

Phage display

Skin

Snail

(detection of 2-O-sulfated iduronate and N-acetylglucosamine units in  
 heparan sulfate by an antibody selected against **acharan**  
**sulfate** (IdoA2S-GlcNAc)n)

IT Antibodies and Immunoglobulins

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(detection of 2-O-sulfated iduronate and N-acetylglucosamine units in  
 heparan sulfate by an antibody selected against **acharan**  
**sulfate** (IdoA2S-GlcNAc)n)

IT 7512-17-6, N-Acetylglucosamine 9050-30-0 192662-57-0,  
**Acharan sulfate**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(detection of 2-O-sulfated iduronate and N-acetylglucosamine units in  
heparan sulfate by an antibody selected against **acharan**  
**sulfate** (IdoA2S-GlcNAc)n)

IT 177791-14-9  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(repeating unit, detection of 2-O-sulfated iduronate and  
N-acetylglucosamine units in heparan sulfate by an antibody selected  
against **acharan sulfate** (IdoA2S-GlcNAc)n)

IT 192662-57-0, **Acharan sulfate**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(detection of 2-O-sulfated iduronate and N-acetylglucosamine units in  
heparan sulfate by an antibody selected against **acharan**  
**sulfate** (IdoA2S-GlcNAc)n)

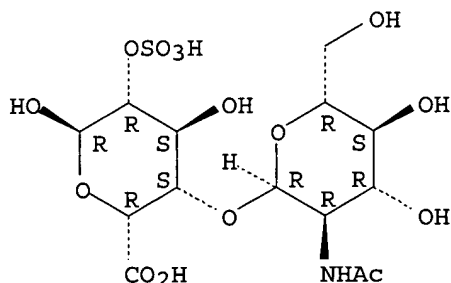
RN 192662-57-0 CAPLUS  
CN Acharan, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 177791-14-9  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(repeating unit, detection of 2-O-sulfated iduronate and  
N-acetylglucosamine units in heparan sulfate by an antibody selected  
against **acharan sulfate** (IdoA2S-GlcNAc)n)

RN 177791-14-9 CAPLUS  
CN  $\alpha$ -L-Idopyranuronic acid, 4-O-[2-(acetylamino)-2-deoxy- $\alpha$ -D-  
glucopyranosyl]-, 2-(hydrogen sulfate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L174 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2  
ACCESSION NUMBER: 2004:924013 CAPLUS  
DOCUMENT NUMBER: 142:109434  
TITLE: Novel **acharan sulfate** lyases  
specifically degrading **acharan**  
**sulfate**, preparing method and use thereof  
INVENTOR(S): Kim, Byeong Taek; Kim, Dong Hyun; Kim, Wan Seok; Kim,  
Young Sik  
PATENT ASSIGNEE(S): S. Korea  
SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given  
CODEN: KRXXA7  
DOCUMENT TYPE: Patent  
LANGUAGE: Korean  
FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE     |
|------------------------|------|----------|-----------------|----------|
| KR 2002046294          | A    | 20020621 | KR 2000-75605   | 20001212 |
| PRIORITY APPLN. INFO.: |      |          | KR 2000-75605   | 20001212 |

AB Novel **acharan** sulfate lyases specifically degrading **acharan** sulfate, a preparing method and a use thereof are provided, therefore the **acharan** sulfate lyase having improved substrate specificity and stability can be produced and it can be useful in producing **acharan** sulfate oligosaccharides inhibiting the metastasis of **cancer**. The **acharan** sulfate lyase capable of degrading glycosaminoglycans (GAG) is isolated from *Bacteroides stercoris* HJ-15, wherein glycosaminoglycans (GAG) are **acharan** sulfate, heparin and heparan sulfate; the **acharan** sulfate lyase has 82,500 Da of mol. weight and optimal pH of 7.0 to 7.2 and optimal temperature of 42 to 45 deg. C; and the activity of enzyme is increased by Mg<sup>2+</sup> or Mn<sup>2+</sup> and inhibited by Cu<sup>2+</sup> or Ni<sup>2+</sup>. The method for producing the **acharan** sulfate lyase comprises the steps of: culturing *Bacteroides stercoris* in an appropriate medium; recovering the cultured cells and preparing cell extract; and subjecting the cell extract to chromatog., wherein the chromatog. is selected from QAE-cellulose, DEAE-cellulose, CM-Sephadex C-50, hydroxyapatite, CM-Sephadex C-25 and Hi-Trap SP.

IC ICM C12N009-88

CC 7-1 (Enzymes)

Section cross-reference(s): 1, 9, 10

ST *Bacteroides* **acharan** sulfate lyase glycosaminoglycan degrdn

IT **Neoplasms**  
(metastasis, inhibition; novel **acharan** sulfate lyases specifically degrading **acharan** sulfate, preparing method and use thereof)

IT **Antitumor agents**  
*Bacteroides stercoris*  
Purification  
(novel **acharan** sulfate lyases specifically degrading **acharan** sulfate, preparing method and use thereof)

IT Glycosaminoglycans, processes  
RL: BCP (Biochemical process); BIOL (Biological study); PROC (Process)  
(novel **acharan** sulfate lyases specifically degrading **acharan** sulfate, preparing method and use thereof)

IT 9005-49-6, Heparin, processes 9050-30-0 192662-57-0, **Acharan sulfate**  
RL: BCP (Biochemical process); BIOL (Biological study); PROC (Process)  
(novel **acharan** sulfate lyases specifically degrading **acharan** sulfate, preparing method and use thereof)

IT 216503-91-2P, **Acharan sulfate** lyase  
RL: BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)  
(novel **acharan** sulfate lyases specifically degrading **acharan** sulfate, preparing method and use thereof)

IT 192662-57-0, **Acharan sulfate**  
RL: BCP (Biochemical process); BIOL (Biological study); PROC (Process)  
(novel **acharan** sulfate lyases specifically

degrading **acharan sulfate**, preparing method and use thereof)

RN 192662-57-0 CAPLUS

CN Acharan, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L174 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2002:813649 CAPLUS

DOCUMENT NUMBER: 138:314215

TITLE: Inhibition by **acharan** sulphate of **angiogenesis** in experimental inflammation models

AUTHOR(S): Ghosh, Ajoy Kumar; Hirasawa, Noriyasu; Lee, Yeon Sil; Kim, Yeong Sik; Shin, Kuk Hyun; Ryu, Nama; Ohuchi, Kazuo

CORPORATE SOURCE: Laboratory of Pathophysiological Biochemistry, Graduate School of Pharmaceutical Sciences, Tohoku University, Miyagi, 980-8578, Japan

SOURCE: British Journal of Pharmacology (2002), 137(4), 441-448

CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 1 The effects of **acharan** sulfate, a glycosaminoglycan isolated from the giant African snail *Achatina fulica*, on **angiogenesis** in the granulation tissue were analyzed using an air pouch-type carrageenin-induced inflammation model in rats and a cotton thread-induced inflammation model in mice. 2 In the carrageenin-induced inflammation model in rats, intra-pouch injections of **acharan** sulfate (5 and 50 µg) inhibited the pouch fluid accumulation and the granulation tissue formation as well as the **angiogenesis** in the granulation tissue at day 6 in a dose-dependent manner. 3 The inhibitory effects of **acharan** sulfate at 50 µg on the pouch fluid accumulation and the leukocyte infiltration into the pouch fluid was not so effective as that of the cyclo-oxygenase inhibitor indomethacin at 100 µg, but the inhibitory effects of **acharan** sulfate at 50 µg on the granulation tissue formation and **angiogenesis** in the granulation tissue were almost the same as those of indomethacin at 100 µg. 4 **Acharan** sulfate did not affect levels of vascular endothelial growth factor (VEGF) in the granulation tissue and in the pouch fluid at day 6, but indomethacin significantly lowered them. 5 In the cotton thread-induced inflammation model in mice, injections of **acharan** sulfate (10 µg) at the site of the cotton thread implantation inhibited the granulation tissue formation and **angiogenesis** as indomethacin (20 µg) did. **Acharan** sulfate (10 µg) did not affect levels of VEGF in the cotton thread-induced granulation tissue at day 5, but indomethacin (20 µg) significantly lowered them. 6 In culture of human vascular endothelial cells, **acharan** sulfate at 10 and 100 µg ml<sup>-1</sup> inhibited VEGF-induced capillary tube formation. 7 These findings suggest that the inhibitory effect of **acharan** sulfate on **angiogenesis** in carrageenin- and cotton thread-induced granulation tissues is not due to the inhibition of VEGF protein induction, but is due to the inhibition of VEGF-induced vascular tube formation.

CC 1-8 (Pharmacology)

ST **acharan sulfate angiogenesis** inhibitor  
inflammation VEGF

IT Blood vessel

(endothelium; inhibition by **acharan sulfate** of  
**angiogenesis** in exptl. inflammation models)

IT **Angiogenesis**  
**Angiogenesis** inhibitors  
 Capillary vessel  
 Human  
 Inflammation  
 (inhibition by **acharan sulfate** of  
**angiogenesis** in exptl. inflammation models)

IT Endothelium  
 (vascular; inhibition by **acharan sulfate** of  
**angiogenesis** in exptl. inflammation models)

IT 106096-93-9, Basic fibroblast growth factor 127464-60-2, Vascular  
 endothelial growth factor  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibition by **acharan sulfate** of  
**angiogenesis** in exptl. inflammation models)

IT 53-86-1, Indomethacin 145-63-1, Suramin 192662-57-0,  
**Acharan sulfate**  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (inhibition by **acharan sulfate** of  
**angiogenesis** in exptl. inflammation models)

IT 192662-57-0, **Acharan sulfate**  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (inhibition by **acharan sulfate** of  
**angiogenesis** in exptl. inflammation models)

RN 192662-57-0 CAPLUS

CN Acharan, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L174 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:79185 CAPLUS

DOCUMENT NUMBER: 144:150592

TITLE: Preparation of aza uronic acids as heparanase  
 inhibitors and **antitumor** and  
 antiinflammatory agents

INVENTOR(S): Petitou, Maurice; Driguez, Pierre Alexandre

PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.

SOURCE: Fr. Demande, 72 pp.

CODEN: FRXXBL

DOCUMENT TYPE: Patent

LANGUAGE: French

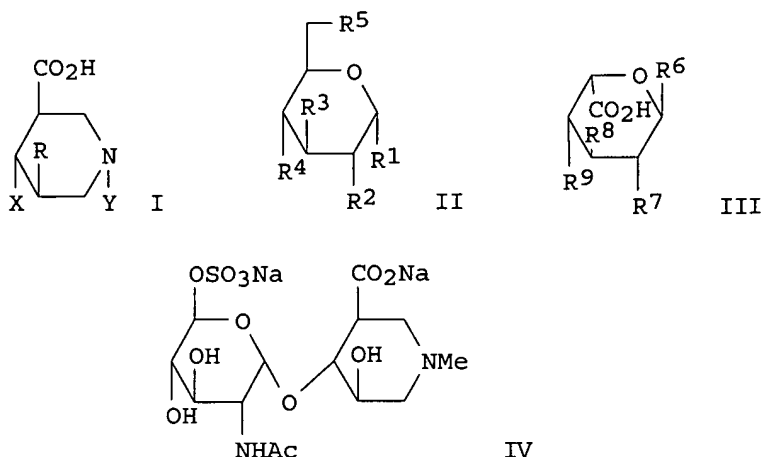
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE     |
|------------------------|------|----------|-----------------|----------|
| FR 2873377             | A1   | 20060127 | FR 2004-8160    | 20040723 |
| PRIORITY APPLN. INFO.: |      |          | FR 2004-8160    | 20040723 |

GI





AB Title aza sugars I, wherein R is H, OH, OSO<sub>3</sub>H, acyl, O-aralkyl; X is OH, formula II, wherein R<sub>1</sub> is O-sugar residue; R<sub>2</sub> is NH<sub>2</sub>, NHCO-alkyl, NHCO-aryl, NHSO<sub>3</sub>H, OH, O-alkyl, O-aralkyl, OSO<sub>3</sub>H; R<sub>3</sub> is OH, OSO<sub>3</sub>H, O-alkyl, O-aralkyl; R<sub>4</sub> is OH, OSO<sub>3</sub>H, O-alkyl, O-aralkyl, sugar formula III, wherein R<sub>6</sub> is O-sugar residue; R<sub>7</sub> and R<sub>8</sub> are independently same as R<sub>3</sub>; R<sub>9</sub> is OH, OSO<sub>3</sub>H, O-alkyl, O-aralkyl, sugar residue; Y is H, alkyl, sugar residue, uronic acid residue, were prepared and used as as heparanase inhibitors and **antitumor** and antiinflammatory agents. Thus, disaccharide uronic acid II was prepared and used as heparanase inhibitor and **antitumor** and antiinflammatory agent (no data).

CC 33-8 (Carbohydrates)

Section cross-reference(s): 1, 7, 63

ST aza uronic acid prepn heparanase inhibitor **antitumor**  
antiinflammatory drug

IT Anti-inflammatory agents  
**Antitumor** agents

Drugs

(preparation of aza uronic acids as heparanase inhibitors and  
**antitumor** and antiinflammatory agents)

IT Disaccharides  
Uronic acids

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aza uronic acids as heparanase inhibitors and  
**antitumor** and antiinflammatory agents)

IT 89800-66-8, Heparanase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(preparation of aza uronic acids as heparanase inhibitors and  
**antitumor** and antiinflammatory agents)

IT **873664-70-1P** 873664-71-2P 873664-72-3P **873664-73-4P**  
873664-77-8P 873664-96-1P 873665-17-9P 873665-21-5P 873665-32-8P  
873665-33-9P 873665-34-0P 873665-38-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aza uronic acids as heparanase inhibitors and  
**antitumor** and antiinflammatory agents)

IT 67313-50-2 103703-07-7 114869-97-5 131522-43-5 135415-92-8  
873664-53-0 873664-81-4 873664-99-4

RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of aza uronic acids as heparanase inhibitors and  
**antitumor** and antiinflammatory agents)

IT 215725-53-4P 873664-54-1P 873664-55-2P 873664-56-3P 873664-57-4P  
873664-58-5P 873664-59-6P 873664-60-9P 873664-61-0P 873664-62-1P  
873664-63-2P 873664-64-3P 873664-65-4P 873664-66-5P 873664-67-6P  
873664-68-7P **873664-69-8P** 873664-74-5P 873664-75-6P  
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873839-14-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation of aza uronic acids as heparanase inhibitors and  
**antitumor** and antiinflammatory agents)

IT 873665-39-5P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of aza uronic acids as heparanase inhibitors and  
**antitumor** and antiinflammatory agents)

IT **873664-70-1P 873664-73-4P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
(Uses)

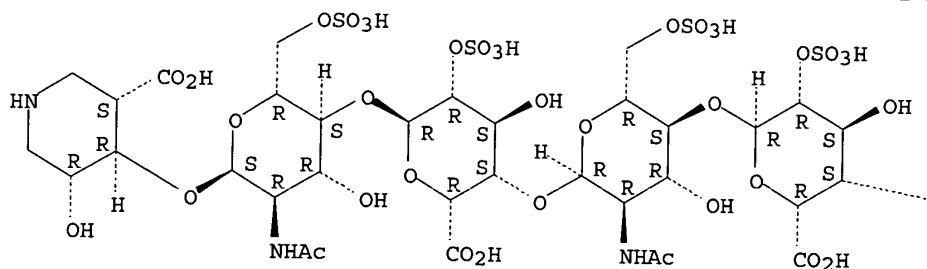
(preparation of aza uronic acids as heparanase inhibitors and  
**antitumor** and antiinflammatory agents)

RN 873664-70-1 CAPLUS

CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.

PAGE 1-A



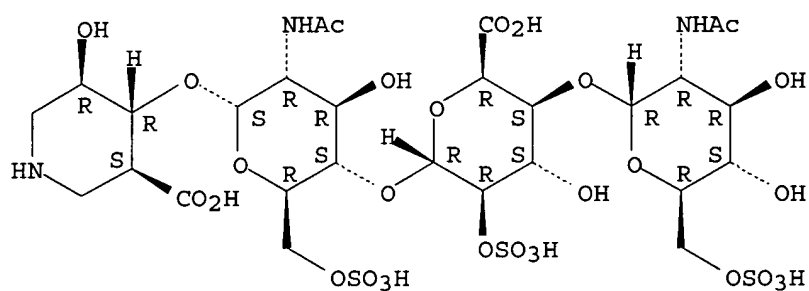
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PAGE 1-B

.....OSO<sub>3</sub>H

RN 873664-73-4 CAPLUS  
 CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.

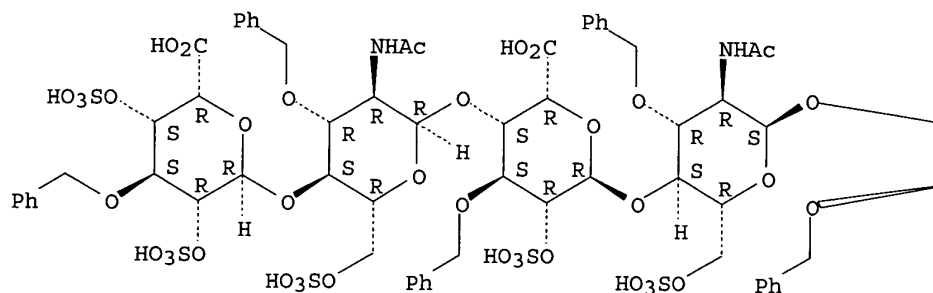


●5 Na

IT 873664-69-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation of aza uronic acids as heparanase inhibitors and  
**antitumor** and antiinflammatory agents)  
 RN 873664-69-8 CAPLUS  
 CN INDEX NAME NOT YET ASSIGNED

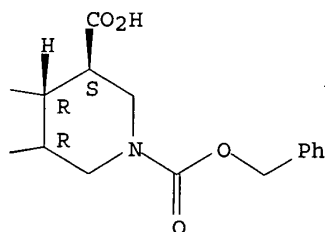
Absolute stereochemistry.

PAGE 1-A



● 8 Na

PAGE 1-B



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L174 ANSWER 5 OF 8 MEDLINE on STN  
 ACCESSION NUMBER: 2000014519 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 10545209  
 TITLE: Effect of fully sulfated glycosaminoglycans on pulmonary artery smooth muscle cell proliferation.  
 AUTHOR: Garg H G; Joseph P A; Thompson B T; Hales C A; Toida T; Imanari T; Capila I; Linhardt R J  
 CORPORATE SOURCE: Pulmonary/Critical Care Unit, Massachusetts General Hospital, Boston, Massachusetts 02114, USA.. hgarg@partners.org  
 SOURCE: Archives of biochemistry and biophysics, (1999 Nov 15) 371 (2) 228-33.  
 Journal code: 0372430. ISSN: 0003-9861.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199912

ENTRY DATE: Entered STN: 20000113  
Last Updated on STN: 20000113  
Entered Medline: 19991221

## ABSTRACT:

Fully sulfated heparin and other glycosaminoglycans, namely heparan, chondroitin, and dermatan sulfates, and hyaluronan have been prepared by using sulfur trioxide under mild chemical conditions. All these derivatives were assayed for antiproliferative activity on cultured bovine pulmonary artery smooth muscle cells (BPASMCs). No appreciable difference was found between heparin and fully sulfated heparin. Chondroitin and dermatan sulfates actually stimulated BPASMCs growth but full sulfonation made them strongly antiproliferative. Native hyaluronan was not antiproliferative but became strongly so after sulfonation. Neither **acharan sulfate** nor **\*\*\*N\*\*\* -sulfoacharan sulfate** had any antiproliferative activity. This suggests that O-sulfonation of the polysaccharide is critical for antiproliferative activity, whereas N-sulfonation of glucosamine residues is not.

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CONTROLLED TERM: Check Tags: Comparative Study  
Animals  
\*Antineoplastic Agents: PD, pharmacology  
Carbohydrate Sequence  
Cattle  
Cells, Cultured  
Glycosaminoglycans: CH, chemistry  
\*Glycosaminoglycans: PD, pharmacology  
Molecular Sequence Data  
\*Muscle, Smooth, Vascular: DE, drug effects  
\*Pulmonary Artery: CY, cytology  
Sequence Analysis  
CAS REGISTRY NO.: 64082-61-7 (A73025)  
CHEMICAL NAME: 0 (Antineoplastic Agents); 0 (Glycosaminoglycans)

L174 ANSWER 6 OF 8 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN  
ACCESSION NUMBER: 2006-100079 [10] WPIX  
DOC. NO. CPI: C2006-035709  
TITLE: New oligosaccharide compounds are neuronal growth modulators useful to treat neurological disorder (CNS lesions, gliosis, Parkinson's disease, Alzheimer's disease, neuronal degeneration or spinal cord trauma).  
DERWENT CLASS: A11 A14 A96 B02 B04  
INVENTOR(S): GAMA, C I; HSIEH-WILSON, L C; MABON, R; TULLY, S E  
PATENT ASSIGNEE(S): (GAMA-I) GAMA C I; (HSIE-I) HSIEH-WILSON L C; (MABO-I) MABON R; (TULL-I) TULLY S E; (CALY) CALIFORNIA INST OF TECHNOLOGY  
COUNTRY COUNT: 111  
PATENT INFORMATION:

| PATENT NO   | KIND DATE             | WEEK | LA | PG |
|---|-----------------------|------|----|----|
| WO 2005118609   | A2 20051215 (200610)* | EN   | 89 |    |
| RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT |                       |      |    |    |
| KE LS LT LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG     |                       |      |    |    |
| ZM ZW   |                       |      |    |    |
| W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE  |                       |      |    |    |
| DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG     |                       |      |    |    |
| KM KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NG NI     |                       |      |    |    |

NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SM SY TJ TM TN TR TT  
 TZ UA UG US UZ VC VN YU ZA ZM ZW  
 US 2006025379 A1 20060202 (200610)

## APPLICATION DETAILS:

| PATENT NO     | KIND           | APPLICATION     | DATE     |
|---------------|----------------|-----------------|----------|
| WO 2005118609 | A2             | WO 2005-US18906 | 20050526 |
| US 2006025379 | A1 Provisional | US 2004-574433P | 20040526 |
|               |                | US 2005-140618  | 20050526 |

PRIORITY APPLN. INFO: US 2004-574433P 20040526; US  
 2005-140618 20050526

AN 2006-100079 [10] WPIX

AB WO2005118609 A UPAB: 20060209

NOVELTY - Oligosaccharide compounds (I) and their derivatives are new.  
 DETAILED DESCRIPTION - Oligosaccharide compounds of formula (I) and their derivatives are new.

R1-R4 = H, sulfate, phosphate or carboxylate;

R5 = alkyl or alkenyl (both optionally substituted); and

n = 0-100.

INDEPENDENT CLAIMS are also included for:

(1) a polysaccharide compound containing a repeating dimer unit of formula (IIa);

(2) a substantially pure compound (I);

(3) a oligosaccharide compound (III) of formula (R-L-R);

(4) a glycopolymer (IV) comprising a polymer backbone P conjugated with a R via a linker L (P is a polymer (polyacrylamide, polyacrylate of poly(N-acryloxy)succinimide));

(5) a method of inducing growth of differentiated neural stem cells comprising administration of (I);

(6) a method for screening for small molecule inducers of neuronal growth comprising applying to a cultured neuron a small molecule of (I) and determining an increase in percent growth in axon length of treated versus untreated neuron; and

(7) an article of manufacture comprising packaging material (I).

R = oligosaccharide compound of formula (IIIa); and

L = bifunctional linker molecule

Provided that R1-R4 is not H, when R1 is sulfate, then R2 is not OH, when R2 is sulfate, then R1 is not OH.

ACTIVITY - Neuroprotective; CNS-Gen.; Antiparkinsonian; Nootropic; Vulnerary.

MECHANISM OF ACTION - Neuronal growth modulator; Fibroblast growth factor modulator.

The ability of (I) to modulate neuronal growth was tested using biological assays. The results showed that (I) promotes outgrowth of cultured dopaminergic and DRG neurons by 30-40% relative to the untreated controls.

USE - (I) is useful: to treat a neurological disorder (central nervous system lesions, gliosis, Parkinson's disease, Alzheimer's disease, neuronal degeneration or spinal cord trauma); and promotes regeneration of an injured or severed nerve or nerve tissue or promotes outgrowth in a neuronal cell (brain, CNS or peripheral nerves) and neuronal growth in a cultured neuron (hippocampal neurons, dopaminergic neurons or dorsal root ganglion neuron) (claimed).

ADVANTAGE - (I) is substantially pure (claimed).

Dwg.0/7

DCSE 1239692-1-0-0

SDCN RALA6S

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

L174 ANSWER 7 OF 8 USPATFULL on STN

ACCESSION NUMBER: 2006:28545 USPATFULL  
TITLE: Small molecule stimulators of neuronal growth  
INVENTOR(S): Hsieh-Wilson, Linda C., San Marino, CA, UNITED STATES  
Tully, Sarah E., Pasadena, CA, UNITED STATES  
Mabon, Ross, Princeton, NJ, UNITED STATES  
Gama, Cristal I., Los Angeles, CA, UNITED STATES

|                     | NUMBER         | KIND | DATE          |
|---------------------|----------------|------|---------------|
| PATENT INFORMATION: | US 2006025379  | A1   | 20060202      |
| APPLICATION INFO.:  | US 2005-140618 | A1   | 20050526 (11) |

|                       | NUMBER  | DATE          |
|-----------------------|---|---------------|
| PRIORITY INFORMATION: | US 2004-574433P   | 20040526 (60) |
| DOCUMENT TYPE:        | Utility   |               |
| FILE SEGMENT:         | APPLICATION   |               |
| LEGAL REPRESENTATIVE: | FISH & RICHARDSON, PC, P.O. BOX 1022, MINNEAPOLIS, MN, 55440-1022, US |               |
| NUMBER OF CLAIMS:     | 57  |               |
| EXEMPLARY CLAIM:      | 1   |               |
| NUMBER OF DRAWINGS:   | 7 Drawing Page(s)   |               |
| LINE COUNT:           | 2411  |               |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Provided herein are small molecule stimulators of neuronal growth, their preparation, and their use for treatment of neurological disorders. In one embodiment, provided herein are methods of treatment, prevention, or amelioration of a variety of medical conditions associated with neurological disorders using the compounds and compositions provided herein.

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SUMM . . . the growth of the implanted tissue. In certain embodiments, the compounds provided herein interact with growth factors and cytokines (e.g., **tumor** necrosis factor- $\alpha$  or TNF $\alpha$  and nerve growth factor or NGF).

DRWD FIG. 5 illustrates binding selectivity of tetrasaccharides CS-E and CS-C, and dimer CS-E to **tumor** necrosis factor- $\alpha$ .

DETD In one embodiment, liposomal suspensions, including tissue-targeted liposomes, such as **tumor**-targeted liposomes, may also be suitable as pharmaceutically acceptable carriers. These may be prepared according to methods known to those skilled. . .

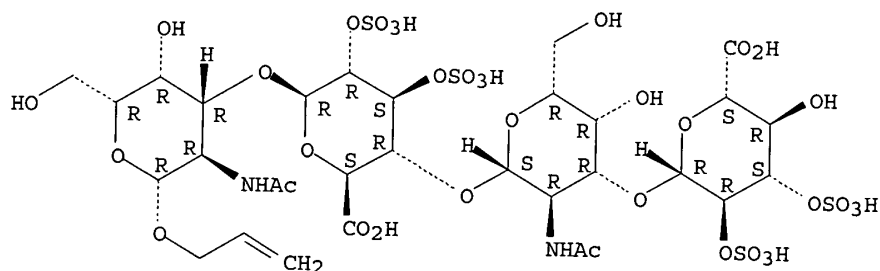
DETD . . . 30-40% relative to the untreated controls. FIGS. 5 and 7 illustrate binding of tetrasaccharides CS-E, CS-C and disaccharide CS-E to **tumor** necrosis factor- $\alpha$  and midkine, respectively.

DETD . . . proteins or other factors that stimulate the growth. In certain embodiments, the compounds provided herein are administered in combination with **tumor** necrosis factor- $\alpha$  or TNF $\alpha$  and nerve growth factor or NGF. In certain embodiments, the compounds

provided herein interact with growth factors and cytokines (e.g., tumor necrosis factor- $\alpha$  or TNF $\alpha$  and nerve growth factor or NGF).

IT 727991-33-5P 727991-35-7P 866719-13-3P 871095-82-8P 871095-83-9P  
**871095-84-0P**  
 (preparation of acetamidodeoxy-oligosaccharide uronic acids as small mol. stimulators of neuronal growth)  
 IT **871095-84-0P**  
 (preparation of acetamidodeoxy-oligosaccharide uronic acids as small mol. stimulators of neuronal growth)  
 RN 871095-84-0 USPATFULL  
 CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



● 6 Na

L174 ANSWER 8 OF 8 USPATFULL on STN  
 ACCESSION NUMBER: 2003:238439 USPATFULL  
 TITLE: Method for linking nucleic acids and/or glycosaminoglycans to polar/hydrophilic materials  
 INVENTOR(S): Van Kuppevelt, Antonius H M S M, Nijmegen, NETHERLANDS  
 Veerkamp, Jacobus Henricus, Nijmegen, NETHERLANDS  
 Blank, Thiemo Arnim, Plankstadt, GERMANY, FEDERAL REPUBLIC OF

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CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to a method for linking nucleic acid and/or glycosaminoglycan or glycosaminoglycan mimetics to a polar/hydrophilic material, characterized by contacting a nucleic acid and/or glycosaminoglycan and a polar/hydrophilic material with each other in the presence of a solution being 20 to 100 percent saturated with a non-chaotropic salt and removing said solution from the nucleic acid and/or glycosaminoglycan--polar/hydrophilic material.

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DETD . . . disaccharide. Within the meaning of the present invention, glycosaminoglycans include heparin, heparan sulfate, hyaluronate, chondroitin sulfate, dermatan sulfate, chitosan sulfate **acharan sulfate** and keratan sulfate and derivatives thereof.

DETD . . . deliver radioactive compounds to a speicific site in the body for radiological treatment of diseases such as various forms of **cancer**.

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